(8) 1818-22.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970523
Last Updated on STN: 19970523
Entered Medline: 19970509

AB The amino acid motif QKRAA, when expressed on HLA-DRB1, carries susceptibility to develop **rheumatoid arthritis**. This motif is the basis of strong B and T cell epitopes. Furthermore, it is highly overrepresented in protein databases, suggesting that it carries a function of its own. To identify this function, we used QKRAA peptide affinity columns to screen total protein extracts from **Escherichia** coli. We found that DnaK, the E. coli 70-kD heat shock protein, binds QKRAA. Of interest, DnaK has a natural ligand, **DnaJ**, that contains a QKRAA motif. We found that QKRAA-containing peptides inhibit the binding of DnaK to **DnaJ**. Furthermore, rabbit antibody to the QKRAA motif can inhibit binding of **DnaJ** to DnaK. These data suggest that QKRAA mediates the binding of E. coli chaperone **DnaJ** to its partner chaperone DnaK.

L13 ANSWER 16 OF 34 SCISEARCH COPYRIGHT 2003 THOMSON ISI

ACCESSION NUMBER: 97:607972 SCISEARCH
THE GENUINE ARTICLE: XQ280

TITLE: Genetic bias in immune responses to a cassette shared by different microorganisms in patients with **rheumatoid arthritis**

AUTHOR: LaCava A (Reprint); Nelson J L; Ollier W E R; MacGregor A; Keystone E C; Thorne J C; Scavulli J F; Berry C C; Carson D A; Albani S

CORPORATE SOURCE: UNIV CALIF SAN DIEGO, DEPT MED, 9500 GILMAN DR, LA JOLLA, CA 92093 (Reprint); UNIV CALIF SAN DIEGO, DEPT PEDIAT, LA JOLLA, CA 92093; UNIV CALIF SAN DIEGO, SAM & ROSE STEIN INST RES AGING, LA JOLLA, CA 92093; UNIV CALIF SAN DIEGO, DEPT FAMILY & PREVENT MED, LA JOLLA, CA 92093; FRED HUTCHINSON CANC RES CTR, DIV IMMUNOGENET, SEATTLE, WA 98104; UNIV MANCHESTER, ARC, EPIDEMIOL RES UNIT, MANCHESTER M13 9PT, LANCS, ENGLAND; ST THOMAS HOSP, TWIN RES UNIT, LONDON, ENGLAND; WELLESLEY HOSP, RHEUMAT DIS UNIT, TORONTO, ON M4Y 1J3, CANADA; KAISER PERMANENTE HOSP, SAN DIEGO, CA 92120

COUNTRY OF AUTHOR: USA; ENGLAND; CANADA

SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (1 AUG 1997) Vol. 100, No. 3, pp. 658-663.
Publisher: ROCKEFELLER UNIV PRESS, 1114 FIRST AVE, 4TH FL, NEW YORK, NY 10021.
ISSN: 0021-9738.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 23

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **Rheumatoid arthritis** (**RA**) is an

autoimmune disease associated with HLA-DR beta 1 alleles which contain the QKRAA amino acid sequence in their third hypervariable region(s), The QKRAA sequence is also expressed by several human pathogens, We have shown previously that an **Escherichia** coli peptide encompassing QKRAA is a target of immune responses in **RA** patients, Here we address two questions: first, whether QKRAA may function as an ''immunological cassette'' with similar, **RA**-associated, immunogenic properties when expressed by other common human pathogens; and second, what is the influence of genetic background in the generation of these responses, We find that early **RA** patients have enhanced humoral and cellular immune responses to Epstein-Barr virus and Brucella ovis and Lactobacillus lactis antigens which contain the QKRAA sequence, These results suggest that the QKRAA sequence is an antigenic epitope on several different microbial proteins, and that **RA** patients recognize the immunological cassette on different backgrounds, ANOVA of immune responses to ''shared epitope'' antigens in monozygotic twin couples shows that, despite significantly elevated responses in affected individuals, a similarity between pairs is retained, thus suggesting a role played either by hereditary or shared environmental factors in the genesis or maintenance of these responses.

L13 ANSWER 17 OF 34 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:158261 BIOSIS
DOCUMENT NUMBER: PREV199800158261
TITLE: Isolation and characterization of an IgG monoclonal anti-**dnaJ** antibody from a patient with **rheumatoid arthritis.**
AUTHOR(S): Chukwuocha, Reginald U. (1); Zhang, Baoping (1); Lai, Chung-Jeng (1); Scavulli, John F.; Albani, Salvatore (1); Carson, Dennis A. (1); Chen, Pojen P. (1)
CORPORATE SOURCE: (1) Dep. Med., Calif. San Diego, La Jolla, CA 92093 USA
SOURCE: Arthritis & Rheumatism, (Sept., 1997) Vol. 40, No. 9 SUPPL., pp. S253.
Meeting Info.: 61st National Scientific Meeting of the American College of Rheumatology and the 32nd National Scientific Meeting of the Association of Rheumatology Health Professionals Washington, DC, USA November 8-12, 1997 Association of Rheumatology Health Professionals
. ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L13 ANSWER 18 OF 34 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 97308805 MEDLINE
DOCUMENT NUMBER: 97308805 PubMed ID: 9165996
TITLE: Absence of peripheral blood T cell responses to "shared epitope' containing peptides in recent onset **rheumatoid arthritis.**
AUTHOR: McColl G J; Hammer J; Harrison L C
CORPORATE SOURCE: Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia.
SOURCE: ANNALS OF THE RHEUMATIC DISEASES, (1997 Apr) 56 (4) 240-6.
Journal code: 0372355. ISSN: 0003-4967.

PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970620
Last Updated on STN: 19970620
Entered Medline: 19970609

AB OBJECTIVES: To determine if peptides containing the 'shared epitope' sequence, QKRAA, from either endogenous, HLA-DR beta 1 (0401), or exogenous, **Escherichia** coli **dnaJ**, sources activate T cells in recent onset **rheumatoid arthritis** (**RA**). METHODS: Peripheral blood mononuclear cell (PBMC) proliferative and whole blood cytokine responses to shared epitope containing peptides from DR beta 1 (0401) and E coli **dnaJ**, to control peptides from DR beta 1 (0402) and hsp40 and to the recall antigen, tetanus toxoid, were tested in 20 untreated, recent onset **RA** subjects, 20 HLA, age, and sex matched healthy controls and 18 other subjects with inflammatory **arthritis**. PBMC proliferative responses to a second E coli **dnaJ** peptide (with the shared epitope at the N-terminus) and two peptides from type II collagen with high affinity for DR4(0401) were tested in a further 16 recent onset RA and 17 control subjects. RESULTS: PBMC proliferation and whole blood interferon gamma or interleukin 10 production in response to the shared epitope containing and control peptides were not different between the disease and control groups. On the other hand, compared with controls, RA subjects had significantly higher proliferation to a collagen II (aa 1307-1319) peptide, but significantly lower proliferation and interferon gamma production to tetanus toxoid. CONCLUSION: Recent onset RA subjects had no demonstrable increase in peripheral blood T cell reactivity to shared epitope containing peptides. However, a proportion had increased T cell reactivity to a peptide of similar length from a candidate RA autoantigen, collagen type II. Their impaired responses to tetanus are in keeping with evidence for general T cell hyporesponsiveness in RA.

L13 ANSWER 19 OF 34 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97232194 EMBASE
DOCUMENT NUMBER: 1997232194
TITLE: **DNAJ** (heat shock protein) / relatedantigens, DR4 and **rheumatoid arthritis**.
AUTHOR: Ahmed A.; Cheung N.T.; Raykundalia C.; Situnayake R.D.; Catty D.
CORPORATE SOURCE: A. Ahmed, Department of Microbiology, University of Karachi, Karachi, Pakistan
SOURCE: Journal of the College of Physicians and Surgeons Pakistan, (1997) 7/2 (49-52).
Refs: 18
ISSN: 1022-386X CODEN: JSPJER
COUNTRY: Pakistan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Rheumatoid arthritis** (**RA**) is an autoimmune disease which primarily occurs in HLA DR4 subjects. Several reports suggest the involvement of heat- shock proteins (HSPs) in **RA**. **DnaJ**, a HSP, of bacteria has been reported to possess a homologue sequence with DR4 haplotype suggesting the possible relationship between **DnaJ**, DR4 and **RA**. We have developed a monoclonal antibody (m-Ab) to **DnaJ** of Mycobacterium tuberculosis. The **DnaJ** antigen was detected in several Gram negative bacteria including **Escherichia** coli, **Salmonella** typhi, **Klebsiella** pneumoniae and Yersinia enterocolitica using the anti-**DnaJ** m-Ab in Western blot analysis. No cross-reactivity was noted with Staphylococcus aureus and Streptococcus pyogenes antigen. Anti-**DnaJ** m-Ab was also found to recognize three distinct antigens 38kDa, 43kDa and 60kDa in the DR4 human cell line. The **RA** patient's serum immune complexes possess the **DnaJ** cross-reactive antigen around 38kDa and 60kDa which is not seen in normal subjects. This finding of homology between epitopes of **DnaJ** and some components of susceptible **RA** patients raises the possibility that induction of an antibody and/or T cell response to **DnaJ** might be implicated in an autoimmune process in which the DR4 is involved. The mechanism by which a shared epitope could increase susceptibility to **RA** is unknown and is likely to be complex.

L13 ANSWER 20 OF 34 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 95:735634 SCISEARCH
THE GENUINE ARTICLE: RX684
TITLE: A HUMAN PROTEIN IS THE ULTIMATE TARGET OF ABNORMAL IMMUNE-RESPONSES TO THE **ESCHERICHIA**-COLI HEAT-SHOCK PROTEIN **DNAJ** IN JUVENILE **RHEUMATOID-ARTHRITIS** (JRA)
AUTHOR: ALBANI S (Reprint); MONTEMAYOR A C; LACAVA A; CARSON D A
CORPORATE SOURCE: UNIV CALIF SAN DIEGO, LA JOLLA, CA, 92093; UNIV PAVIA, I-27100 PAVIA, ITALY
COUNTRY OF AUTHOR: USA; ITALY
SOURCE: ARTHRITIS AND RHEUMATISM, (SEP 1995) Vol. 38, No. 9, Supp. S, pp. 933.
ISSN: 0004-3591.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: No References

L13 ANSWER 21 OF 34 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 96071473 MEDLINE
DOCUMENT NUMBER: 96071473 PubMed ID: 7585093
TITLE: Positive selection in autoimmunity: abnormal immune responses to a bacterial **dnaJ** antigenic determinant in patients with early **rheumatoid arthritis**.
AUTHOR: Albani S; Keystone E C; Nelson J L; Ollier W E; La Cava A; Montemayor A C; Weber D A; Montecucco C; Martini A; Carson D A
CORPORATE SOURCE: Department of Medicine, University of California, San Diego, La Jolla 92093-0663, USA.

CONTRACT NUMBER: AR 07567 (NIAMS)
AR 25443 (NIAMS)
AR 41897 (NIAMS)
+
SOURCE: NATURE MEDICINE, (1995 May) 1 (5) 448-52.
Journal code: 9502015. ISSN: 1078-8956.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 19960124
Last Updated on STN: 19960124
Entered Medline: 19951228

AB A novel 'multistep molecular mimicry' mechanism for induction of **rheumatoid arthritis** (**RA**) by bacterial antigens that activate T lymphocytes previously 'educated' by peptides derived from a class of human histocompatibility antigens is reported here. These antigens have the amino acid sequence QKRAA, which is also present on the **Escherichia** coli heat-shock protein **dnaJ**. Synovial fluid cells of early RA patients have strong immune responses to the bacterial antigen, but cells from normal subjects or controls with other autoimmune diseases do not. The activated T cells may cross-react with autologous **dnaJ** heat-shock proteins that are expressed at synovial sites of inflammation. Our findings may have direct relevance to new strategies for the immune therapy of RA.

L13 ANSWER 22 OF 34 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:521440 BIOSIS
DOCUMENT NUMBER: PREV199598535740
TITLE: A human protein is the ultimate target of abnormal immune responses to the E. coli heat shock protein **dnaJ** in juvenile **rheumatoid arthritis** (JRA.
AUTHOR(S): Albani, Salvatore; Montemayor, Ann C.; La Cava, Antonio; Carson, Dennis A. (1); Massa, Margherita; Ravelli, Angelo; Debenedetti, Fabrizio; Martini, Alberto
CORPORATE SOURCE: (1) Univ. Pavia, Pavia Italy
SOURCE: Arthritis & Rheumatism, (1995) Vol. 38, No. 9 SUPPL., pp. S308.
Meeting Info.: 59th National Scientific Meeting of the American College of Rheumatology and the 30th National Scientific Meeting of the Association of Rheumatology Health Professionals San Francisco, California, USA October 21-26, 1995
ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L13 ANSWER 23 OF 34 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 94201959 MEDLINE
DOCUMENT NUMBER: 94201959 PubMed ID: 8151470
TITLE: Immune responses to the **Escherichia** coli **dnaJ** heat shock protein in juvenile **rheumatoid arthritis** and their correlation with disease activity.

AUTHOR: Albani S; Ravelli A; Massa M; De Benedetti F; Andree G; Roudier J; Martini A; Carson D A
CORPORATE SOURCE: Department of Medicine, University of California, San Diego 92093-0663.
CONTRACT NUMBER: AR25443 (NIAMS)
AR40770 (NIAMS)
SOURCE: JOURNAL OF PEDIATRICS, (1994 Apr) 124 (4) 561-5.
Journal code: 0375410. ISSN: 0022-3476.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199405
ENTRY DATE: Entered STN: 19940523
Last Updated on STN: 19940523
Entered Medline: 19940510

AB Patients with juvenile **rheumatoid arthritis** frequently have abnormal immune responses to the hsp65 class of bacterial heat shock proteins. However, lymphocytes from children with other inflammatory diseases may also recognize hsp65, and the role of these antigens in juvenile **rheumatoid arthritis** remains controversial. We have studied humoral and cellular immune responses to a distinct, recently described bacterial heat shock protein, designated **dnaJ**. The **Escherichia** coli **dnaJ** gene was cloned and expressed, and the purified recombinant protein was used as an antigen. Neither normal children nor children with various chronic inflammatory diseases had lymphocyte proliferative responses to recombinant **dnaJ**. However, lymphocytes from patients with polyarticular, pauciarticular, and systemic manifestations of juvenile **rheumatoid arthritis** responded strongly to the antigen. Cellular immune responses to **dnaJ** were higher in synovial fluid than in blood and higher in children with active disease than in children in remission. These data show that increased immune reactivity to **dnaJ** is characteristic of juvenile **rheumatoid arthritis** and that the magnitude of the immune response is linked to disease activity. The results suggest that an abnormal immune response to antigens on commensal gut bacteria may contribute to the generation of chronic inflammation in juvenile **rheumatoid arthritis**.

L13 ANSWER 24 OF 34 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:3704 BIOSIS
DOCUMENT NUMBER: PREV199598018004
TITLE: Characterization in enteric bacteria of equivalents of E. coli **dnaJ**, a protein that shares with several HLA alleles the QKRAA susceptibility sequence to **rheumatoid arthritis** (**RA.**
AUTHOR(S): Albani, Salvatore; La Cava, Antonio; Schrauder, Andre; Carson, Dennis A.
CORPORATE SOURCE: Univ. Calif. San Diego, La Jolla, CA 92093-0663 USA
SOURCE: Arthritis & Rheumatism, (1994) Vol. 37, No. 9 SUPPL., pp. S169.
Meeting Info.: 58th National Scientific Meeting of the American College of Rheumatology and the 29th National Scientific Meeting of the Association of Rheumatology Health Professionals Minneapolis,

Minnesota, USA October 23-27, 1994
ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L13 ANSWER 25 OF 34 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 94:512813 SCISEARCH
THE GENUINE ARTICLE: PB897
TITLE: INFECTION AND MOLECULAR MIMICRY IN AUTOIMMUNE-DISEASES OF CHILDHOOD
AUTHOR: ALBANI S (Reprint)
CORPORATE SOURCE: UNIV CALIF SAN DIEGO, DEPT PEDIAT, 9500 GILMAN DR, LA JOLLA, CA, 92093 (Reprint); UNIV PAVIA, DEPT PEDIAT, I-27100 PAVIA, ITALY
COUNTRY OF AUTHOR: USA; ITALY
SOURCE: CLINICAL AND EXPERIMENTAL RHEUMATOLOGY, (SEP/OCT 1994) Vol. 12, Supp. 10, pp. S35-S41.
ISSN: 0392-856X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: 35
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The etiopathogenesis of childhood chronic autoimmune disease is, in most cases, unknown. Most likely, several factors overlap in determining the loss of tolerance toward certain autoantigens that become the target of the disease and the main cause of its perpetuation. Infectious agents have often been implicated in the pathogenesis of these diseases, but, to date, compelling evidence for a horizontal transmission or for localized epidemics is lacking. Human pathogens may never the less play a role in determining the loss of tolerance toward certain self-antigens by means of mechanisms other than classic infection. It is common knowledge that human pathogens often express proteins with high antigenic potential with important homologies with human proteins. Evolutionary pressures based upon the necessity of escaping the host's specific immune responses may have determined this phenomenon, called ''molecular mimicry''.

It is reasonable to assert that certain individuals can develop abnormal immune responses upon contact with an antigen that mimics a self-protein. These responses may ultimately lead to self-reactivity and autoimmune disease. In this model of molecular mimicry, self-reactivity is triggered by cross-recognition of a self and an exogenous protein that bear the same sequence. A disease triggered by such a mechanism should present with: i) some form of an acute or chronic autoimmune clinical manifestation; ii) o documented clinical correlation between contact with a human pathogen and the autoimmune disease; iii) immune cross-reaction between a protein from a pathogen and a homologous human protein.

Acute rheumatic fever, Reiter's syndrome and the other reactive arthritides fulfill the above conditions. Our hypothesis is that similar mechanisms may contribute to the pathogenesis of other autoimmune diseases in childhood I will discuss herein our work on juvenile **rheumatoid arthritis** and juvenile dermatomyositis.

L13 ANSWER 26 OF 34 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1994:9416 BIOSIS

DOCUMENT NUMBER: PREV199497022416
TITLE: The QKRAA disease susceptibility sequence for **rheumatoid arthritis** (**RA**) is a B cell epitope shared by the Epstein-Barr virus (EBV) protein gp110 and the E. coli heat shock protein **dnaJ**. Possible implications for disease pathogenesis.
AUTHOR(S): La Cava, A. (1); Andree, G. (1); Roudier, J.; Carson, D. (1); Albani, S. (1)
CORPORATE SOURCE: (1) UCLA, La Jolla, CA 92093-0663 USA
SOURCE: Arthritis and Rheumatism, (1993) Vol. 36, No. 9 SUPPL., pp. S127.
Meeting Info.: 57th Annual Scientific Meeting of the American College of Rheumatology San Antonio, Texas, USA November 7-11, 1993
ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L13 ANSWER 27 OF 34 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 93:639760 SCISEARCH
THE GENUINE ARTICLE: MB816
TITLE: THE QKRAA DISEASE SUSCEPTIBILITY SEQUENCE FOR **RHEUMATOID-ARTHRITIS** (**RA**) IS A B-CELL EPITOPE SHARED BY THE EPSTEIN-BARR-VIRUS (EBV) PROTEIN GP110 AND THE **ESCHERICHIA**-COLI HEAT-SHOCK PROTEIN **DNAJ** POSSIBLE IMPLICATIONS FOR DISEASE PATHOGENESIS
AUTHOR: LACAVA A (Reprint); ANDREE G; ROUDIER J; CARSON D; ALBANI S
CORPORATE SOURCE: UCSD, LA JOLLA, CA, 92093; UNIV AIX MARSEILLE 2, F-13007 MARSEILLE, FRANCE
COUNTRY OF AUTHOR: USA; FRANCE
SOURCE: ARTHRITIS AND RHEUMATISM, (SEP 1993) Vol. 36, No. 9, Supp. S, pp. S127.
ISSN: 0004-3591.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: No References

L13 ANSWER 28 OF 34 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1994:8986 BIOSIS
DOCUMENT NUMBER: PREV199497021986
TITLE: The HLA DR4 Dw4 susceptibility sequence to **rheumatoid arthritis**, as expressed on the E. coli heat shock protein **dnaJ**, is a target of T and B cell responses in patients with **RA**.
AUTHOR(S): Albani, S. (1); Keystone, E.; Ollier, W.; Montecucco, C.; Caporali, R.; Massa, M.; Martini, A.; Roudier, J.; Carson, D.
CORPORATE SOURCE: (1) Univ. Calif. San Diego, La Jolla, CA 92093-0663 USA
SOURCE: Arthritis and Rheumatism, (1993) Vol. 36, No. 9 SUPPL., pp. S55.
Meeting Info.: 57th Annual Scientific Meeting of the

American College of Rheumatology San Antonio, Texas, USA November 7-11, 1993
ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L13 ANSWER 29 OF 34 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 93:639330 SCISEARCH
THE GENUINE ARTICLE: MB816
TITLE: THE HLA DR4 DW4 SUSCEPTIBILITY SEQUENCE TO **RHEUMATOID-ARTHRITIS**, AS EXPRESSED ON THE **ESCHERICHIA**-COLI HEAT-SHOCK PROTEIN **DNAJ**, IS A TARGET OF T-CELL AND B-CELL RESPONSES IN PATIENTS WITH **RA**
AUTHOR: ALBANI S (Reprint); KEYSTONE E; OLLIER W; MONTECUCCO C; CAPORALI R; MASSA M; MARTINI A; ROUDIER J; CARSON D
CORPORATE SOURCE: UNIV CALIF SAN DIEGO, LA JOLLA, CA, 92093; UNIV MARSEILLE, MARSEILLE, FRANCE; UNIV TORONTO, TORONTO M5S 1A1, ONTARIO, CANADA; UNIV MANCHESTER, MANCHESTER M13 9PL, LANCS, ENGLAND; UNIV PAVIA, I-27100 PAVIA, ITALY
COUNTRY OF AUTHOR: USA; FRANCE; CANADA; ENGLAND; ITALY
SOURCE: ARTHRITIS AND RHEUMATISM, (SEP 1993) Vol. 36, No. 9, Supp. S, pp. S55.
ISSN: 0004-3591.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: No References

L13 ANSWER 30 OF 34 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 93223294 MEDLINE
DOCUMENT NUMBER: 93223294 PubMed ID: 8467555
TITLE: **Rheumatoid arthritis**: how well do the theories fit the evidence?.
AUTHOR: McCulloch J; Lydyard P M; Rook G A
CORPORATE SOURCE: Department of Medical Microbiology, UCL Medical School, London, UK.
SOURCE: CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1993 Apr) 92 (1) 1-6. Ref: 59
Journal code: 0057202. ISSN: 0009-9104.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199305
ENTRY DATE: Entered STN: 19930521
Last Updated on STN: 19930521
Entered Medline: 19930513

AB In this brief review, inspired partly by a symposium at the autumn meeting of the British Society for Immunology, 1992, varying hypotheses concerning the etiopathogenesis of **rheumatoid arthritis** (**RA**) are explored and tested against current evidence. Immunogenetic considerations, whilst of interest, have not aided our understanding of the development of this disease.

The association with restricted HLA-DR beta chain hypervariable sequences does not hold true with all cases of RA (but may be related to disease severity) and studies of T cell receptor (TCR) beta chain usage fail to show consistent oligoclonality of infiltrating T cells in the synovial compartment. Etiologies based on triggering by bacteria are also considered: homologies between the 'shared epitope' sequences of HLA-DR1 and DR4 beta chains, **Escherichia** coli **dnaJ** and **Proteus** haemolysin do not indicate any feasible mechanisms for the development of RA, and cannot explain the many cases in which such DR sequences do not occur, though new data from man and animals enhance interest in the role of bowel flora. Finally, the striking parallels between slow bacterial infections and RA, in terms of immunogenetics, pathology, IgG glycosylation abnormalities and autoimmune manifestations, are put forward as circumstantial evidence that such bacterial infections may underly, or trigger, this serious disease.

L13 ANSWER 31 OF 34 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 92105402 MEDLINE
DOCUMENT NUMBER: 92105402 PubMed ID: 1370300
TITLE: The susceptibility sequence to **rheumatoid arthritis** is a cross-reactive B cell epitope shared by the **Escherichia** coli heat shock protein **dnaJ** and the histocompatibility leukocyte antigen DRB10401 molecule.
AUTHOR: Albani S; Tuckwell J E; Esparza L; Carson D A; Roudier J
CORPORATE SOURCE: Department of Medicine, University of California, San Diego, La Jolla, California 92093-0945.
CONTRACT NUMBER: AR25443 (NIAMS)
SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (1992 Jan) 89 (1) 327-31.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199202
ENTRY DATE: Entered STN: 19920302
Last Updated on STN: 19960129
Entered Medline: 19920210

AB Immunological responses to bacterial heat shock proteins have been implicated in the pathogenesis of arthritis in animals and humans. The predicted amino acid sequence of **dnaJ**, a heat shock protein from **Escherichia** coli, contains an 11-amino acid segment that is homologous to the third hypervariable region of the human histocompatibility antigen (HLA) DRB10401 (formerly known as HLA Dw4), the part of the molecule that carries susceptibility to **rheumatoid arthritis**. To test the biological significance of this finding, we expressed and purified recombinant **dnaJ** (rdnaJ), and determined its immunologic cross-reactivity with HLA DRB10401. A rabbit antipeptide antiserum raised against the sequence of the third hypervariable region of HLA DRB10401 specifically bound to '**dnaJ**, thus confirming that a similar sequence is expressed on the bacterial protein. Of greater consequence, an antiserum to the '**dnaJ** protein recognized not only a peptide from the third hypervariable region of

HLA DRB10401, but also the intact HLA DRB10401 polypeptide. Furthermore, the antibody to '**dnaJ** reacted with HLA DRB10401 homozygous B lymphoblasts, but not with HLA DRB11501, DRB10101, DRB10301, and DRB10701 (formerly known as HLA Dw2, DR 1, DR 3, and DR 7, in the same order) homozygous cells. These results demonstrate that exposure to a bacterial heat shock protein can elicit antibodies against the **rheumatoid arthritis** susceptibility sequence in the third hypervariable region of HLA DRB10401.

L13 ANSWER 32 OF 34 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1993:18694 BIOSIS
DOCUMENT NUMBER: PREV199344006894
TITLE: Immune response to the **Escherichia** coli **dnaJ** heat shock protein correlates with disease activity in juvenile **rheumatoid arthritis**.
AUTHOR(S): Albani, Salvatore (1); Ravelli, Angelo; Massa, Margherita; De Benedetti, Fabrizio; Andree, Gregor (1); Roudier, Jean; Martini, Alberto; Carson, Dennis A. (1)
CORPORATE SOURCE: (1) Univ. Calif. San Diego, La Jolla, Calif. 92093-0663
SOURCE: Arthritis & Rheumatism, (1992) Vol. 35, No. 9 SUPPL., pp. S56.
Meeting Info.: 56th Annual Scientific Meeting of the American College of Rheumatology, Atlanta, Georgia, USA, October 11-15, 1992. ARTHRITIS RHEUM
ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L13 ANSWER 33 OF 34 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 92:606647 SCISEARCH
THE GENUINE ARTICLE: JR158
TITLE: IMMUNE-RESPONSE TO THE **ESCHERICHIA**-COLI **DNAJ** HEAT-SHOCK PROTEIN CORRELATES WITH DISEASE-ACTIVITY IN JUVENILE **RHEUMATOID-ARTHRITIS**
AUTHOR: ALBANI S (Reprint); RAVELLI A; MASSA M; DEBENEDETTI F; ANDREE G; ROUDIER J; MARTINI A; CARSON D A
CORPORATE SOURCE: UNIV MARSEILLE, MARSEILLE, FRANCE; UNIV CALIF SAN DIEGO, LA JOLLA, CA, 92093; UNIV PAVIA, IRCCS SAN MATTEO, DEPT PEDIAT, I-27100 PAVIA, ITALY
COUNTRY OF AUTHOR: FRANCE; USA; ITALY
SOURCE: ARTHRITIS AND RHEUMATISM, (SEP 1992) Vol. 35, No. 9, Supp. S, pp. S56.
ISSN: 0004-3591.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: No References

L13 ANSWER 34 OF 34 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1992:18513 BIOSIS
DOCUMENT NUMBER: BR42:6213
TITLE: THE **DNAJ** HEAT SHOCK PROTEIN FROM **ESCHERICHIA**-COLI CROSS REACTS WITH HLA DW4.

AUTHOR(S): ALBANI S; CARSON D A; ROUDIER J
CORPORATE SOURCE: UNIV. CALIF. SAN DIEGO, LA JOLLA, CALIF. 92093-0945.
SOURCE: 55TH ANNUAL MEETING OF THE AMERICAN COLLEGE OF RHEUMATOLOGY, BOSTON, MASSACHUSETTS, USA, NOVEMBER 17-21, 1991. ARTHRITIS RHEUM, (1991) 34 (9 SUPPL), S41.
CODEN: ARHEAW. ISSN: 0004-3591.
DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English

(FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 10:38:14 ON 10 JUL 2003)
L14 4225 S "CARSON D"?/AU
L15 294 S "ALBANI S"?/AU
L16 113 S L14 AND L15
L17 56 S (L14 OR L15 OR L16) AND L7
L18 35 DUP REM L17 (21 DUPLICATES REMOVED)

-Author(s)

L18 ANSWER 1 OF 35 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:273129 BIOSIS
DOCUMENT NUMBER: PREV200100273129
TITLE: Vaccine compositions and methods useful in inducing immune protection against **arthritogenic** peptides involved in the pathogenesis of **rheumatoid arthritis.**
AUTHOR(S): **Carson, Dennis A. (1); Albani, Salvatore**
CORPORATE SOURCE: (1) Del Mar, CA USA
ASSIGNEE: The Regents of the University of California
PATENT INFORMATION: US 6153200 November 28, 2000
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Nov. 28, 2000) Vol. 1240, No. 4, pp. No Pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB Vaccine compositions useful in inducing immune protection in a host against **arthritogenic** peptides involved in the pathogenesis of **rheumatoid arthritis** are disclosed. Each vaccine composition provides antigenic **dnaJp1** peptide (by including the peptide or a polynucleotide which encodes the peptide) and, optionally, other peptide fragments of the microbial **dnaJ** protein and/or human homologs thereof. Methods for identifying persons who are predisposed to develop **rheumatoid arthritis** and methods for use of the inventive vaccines are also disclosed.

L18 ANSWER 2 OF 35 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 2000:950483 SCISEARCH
THE GENUINE ARTICLE: 357JU
TITLE: Direct identification of T cells specific for heat shock protein **dnaJ** peptide crossreactive to the 'shared epitope' in patients with **rheumatoid arthritis**: Proof for molecular mimicry in vivo.
AUTHOR: Prakken B J (Reprint); Samodal R T; Barnett J E E; Giannoni F; Bonnin D; **Albani S**

SOURCE: ARTHRITIS AND RHEUMATISM, (SEP 2000) Vol. 43, No. 9, Supp. [S], pp. 1840-1840.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621.
ISSN: 0004-3591.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 0

L18 ANSWER 3 OF 35 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 1
ACCESSION NUMBER: 1999:453566 HCAPLUS
DOCUMENT NUMBER: 132:11483
TITLE: Isolation of an IgG monoclonal anti-**dnaJ** antibody from an immunoglobulin combinatorial library from a patient with **rheumatoid arthritis**
AUTHOR(S): Chukwuocha, Reginald U.; Zhang, Baoping; Lai, Chung-Jeng; Scavulli, John F.; **Albani, Salvatore; Carson, Dennis A.**; Chen, Pojen P.
CORPORATE SOURCE: Department of Medicine/Rheumatology, University of California, Los Angeles, CA, 90095-1670, USA
SOURCE: Journal of Rheumatology (1999), 26(7), 1439-1445
CODEN: JRHUA9; ISSN: 0315-162X
PUBLISHER: Journal of Rheumatology Publishing Co. Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Previously, we showed that **rheumatoid arthritis** (**RA**) had both antibodies and T cells specific for the QKRAA-encompassing Escherichia coli **dnaJ** protein. These findings suggest that the bacteria induced anti-**dnaJ** responses may cross react with the human homolog of bacterial **dnaJ** in the joint, resulting in tissue damage. We used the combinatorial library technique to isolate and characterize an IgG monoclonal anti-**dnaJ** antibody (designated CG1) from the blood of a patient with RA. Sequence anal. of CG1 revealed that its heavy and light chain V regions were resp. most homologous to the 3d279d VH4 and the O18 Vk1 genes. Interestingly, 3d279d is frequently expressed by B cells stimulated with staphylococcal enterotoxin; and O18 is the main gene employed by the Vk1 IgG antibodies against Haemophilus influenzae. The combinatorial Ig library method represents an interesting model of how to approach the isolation and characterization of antibody-like reagents in the elucidation of autoantigens in RA.
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 35 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 1999:898894 SCISEARCH
THE GENUINE ARTICLE: 242JG
TITLE: An E-coli heat shock protein **dnaJ** peptide homologous to the ''shared epitope'' is a trigger of pro-inflammatory, TH-1 type T cell responses in patients with early **rheumatoid arthritis** (**RA**).
AUTHOR: Prakken B J (Reprint); Samodal R T; Mendivil A;

Bonnin D; Lanza P; Amox D; Roord S A; DeKleer I; Jones M; **Carson D A; Albani S**

SOURCE: ARTHRITIS AND RHEUMATISM, (SEP 1999) Vol. 42, No. 9, Supp. [S], pp. 114-114.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0004-3591.

DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 0

L18 ANSWER 5 OF 35 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:531452 BIOSIS
DOCUMENT NUMBER: PREV199900531452
TITLE: An E. coli heat shock protein **dnaJ** peptide homologous to the "shared epitope" is a trigger of pro-inflammatory, TH-1 type T cell responses in patients with early **rheumatoid arthritis** (**RA**.
AUTHOR(S): Prakken, Berent J. (1); Samodal, Rodrigo T. (1); Mendivil, Albert (1); Bonnin, Dustan (1); Lanza, Paola (1); Amox, Diane (1); Roord, Sarah A. (1); De Kleer, Isme (1); Jones, Megan (1); **Carson, Dennis A. (1); Albani, Salvatore (1)**
CORPORATE SOURCE: (1) La Jolla, CA USA
SOURCE: Arthritis & Rheumatism, (Sept., 1999) Vol. 42, No. 9 SUPPL., pp. S89.
Meeting Info.: 63rd Annual Scientific Meeting of the American College of Rheumatology and the 34th Annual Scientific Meeting of the Association of Rheumatology Health Professionals Boston, Massachusetts, USA November 13-17, 1999
ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L18 ANSWER 6 OF 35 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:243120 HCAPLUS
DOCUMENT NUMBER: 133:236729
TITLE: Immunomodulatory effects by a heat shock protein **dnaJ**-derived peptide in **rheumatoid arthritis**
AUTHOR(S): Samodal, Rodrigo T.; **Albani, Salvatore**
CORPORATE SOURCE: Departments of Medicine and Pediatrics, University of California, San Diego, La Jolla, CA, 92093-0663, USA
SOURCE: Verhandelingen - Koninklijke Nederlandse Akademie van Wetenschappen, Afdeling Natuurkunde, Tweede Reeks (1999), 101(Specific Immunotherapy of Chronic Autoimmune Diseases), 63-71
CODEN: VNAWAG; ISSN: 0373-465X
PUBLISHER: Royal Netherlands Academy of Arts and Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Peptides derived from the E. coli heat shock protein (hsp) **dnaJ** share the "shared epitope" sequence with HLA DR alleles

assocd. with **rheumatoid arthritis**. These peptides are antigenic in human autoimmune arthritis. T cell recognition of these peptides is assocd. with TH-1 type and pro-inflammatory responses, including prodn. of TNF.alpha., suggesting an involvement of these abnormal responses in the pathogenesis of autoimmune inflammation. In a pilot clin. trial, we attempted to modulate these pro-inflammatory responses by oral administration of various doses (.25, 2.5, 25 mg po qd for 6 mo) of the target antigen in 15 patients with **rheumatoid arthritis**. We measured the percentage of CD3+ cells producing the pro-inflammatory cytokines IL2, IFN.gamma., TNF.alpha., and the tolerogenic cytokines IL4 and IL10, by FACS anal. of the intracellular products. In addn., we measured the cytokine concns., including TGF.beta., by ELISA in culture supernatant. The obsd. decline in pro-inflammatory cytokines prodn. during treatment was accompanied by IL4, IL10 and TGF.beta. prodn., suggesting an effective immunomodulation of these disease-specific responses.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 7 OF 35 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:441966 HCAPLUS
DOCUMENT NUMBER: 129:94461
TITLE: Vaccine compositions and methods useful in inducing immune protection against **arthritogenic** peptides involved in the pathogenesis of **rheumatoid arthritis**
INVENTOR(S): **Carson, Dennis A.; Albani, Salvatore**
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: U.S., 18 pp., Cont.-in-part of U. S. Ser. No. 246,988, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5773570	A	19980630	US 1996-618464	19960315
HU 76359	A2	19970828	HU 1996-3214	19950424
HU 220101	B	20011028		
CA 2247804	AA	19970918	CA 1997-2247804	19970220
WO 9734002	A1	19970918	WO 1997-US2957	19970220
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9719755	A1	19971001	AU 1997-19755	19970220
AU 727087	B2	20001130		

EP 923646	A1	19990623	EP 1997-907862	19970220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 331989	A	20000128	NZ 1997-331989	19970220
JP 2000507232	T2	20000613	JP 1997-532622	19970220
US 6153200	A	20001128	US 1998-107615	19980630
NO 9804244	A	19981116	NO 1998-4244	19980914
PRIORITY APPLN. INFO.:			US 1994-246988	B2 19940520
			US 1996-618464	A 19960315
			WO 1997-US2957	W 19970220

AB Vaccine compns. useful in inducing immune protection in a host against **arthritogenic** peptides involved in the pathogenesis of **rheumatoid arthritis** are disclosed. Each vaccine compn. provides antigenic **dnaJp1** peptide (by including the peptide or a polynucleotide which encodes the peptide).

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 8 OF 35 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 1998:268474 SCISEARCH
THE GENUINE ARTICLE: ZE588
TITLE: Mucosal modulation of immune responses to heat shock proteins in autoimmune arthritis
AUTHOR: Bonnin D (Reprint); **Albani S**
CORPORATE SOURCE: UNIV CALIF SAN DIEGO, DEPT PEDIAT, 9500 GILMAN DR, LA JOLLA, CA 92093 (Reprint); UNIV CALIF SAN DIEGO, DEPT MED, LA JOLLA, CA 92093
COUNTRY OF AUTHOR: USA
SOURCE: BIOTHERAPY, (MAR 1998) Vol. 10, No. 3, pp. 213-221. Publisher: KLUWER ACADEMIC PUBL, SPUIBOULEVARD 50, PO BOX 17, 3300 AA DORDRECHT, NETHERLANDS. ISSN: 0921-299X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 39

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Induction of oral tolerance to antigens that are targets of self-reactive immune responses is an attractive approach to antigen-specific immune therapy of autoimmune diseases. Oral tolerization has indeed proven to be safe and effective in amelioration of autoimmune diseases in animal models, In humans, results have been somewhat controversial. The emphasis given to clinical outcome rather than to immunomodulation, and the difficulty in identifying appropriate candidate antigens contribute to the controversy. Heat shock proteins are promising targets for immune intervention. Immune reactivity to heat shock proteins has indeed been correlated with autoimmune arthritis in animal models, and abnormal immune responses to heat shock proteins have been described in human arthritis as well. Despite significant recent progress, little is known at a molecular level regarding the mechanisms which are responsible for a switch from autoimmunity to tolerance in humans. This is particularly true with respect to sequential analysis of several molecular and immunologic markers during both the course and treatment of disease. Novel approaches are currently under way to fill the gaps. We will briefly detail here the

experience gained to date, and identify some of the avenues which future research will explore.

L18 ANSWER 9 OF 35 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 2
ACCESSION NUMBER: 1997:625612 HCAPLUS
DOCUMENT NUMBER: 127:277197
TITLE: Antigens for use in inducing immune tolerance to **arthritogenic** peptides and protection against **rheumatoid arthritis**
INVENTOR(S): **Carson, Dennis A.; Albani, Salvatore**
PATENT ASSIGNEE(S): Regents of the University of California, USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9734002	A1	19970918	WO 1997-US2957	19970220
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5773570	A	19980630	US 1996-618464	19960315
AU 9719755	A1	19971001	AU 1997-19755	19970220
AU 727087	B2	20001130		
EP 923646	A1	19990623	EP 1997-907862	19970220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 331989	A	20000128	NZ 1997-331989	19970220
JP 2000507232	T2	20000613	JP 1997-532622	19970220
NO 9804244	A	19981116	NO 1998-4244	19980914

PRIORITY APPLN. INFO.:
US 1996-618464 A 19960315
US 1994-246988 B2 19940520
WO 1997-US2957 W 19970220

AB Peptides that can be used in compns. that induce immune tolerance to peptides contg. the sequence Q(K/R)RAA that is found in some HLA proteins are described. This induces tolerance to a range of **arthritogenic** peptides involved in the pathogenesis of **rheumatoid arthritis**. Specifically, the **arthritogenic** peptides are derived from the **DnaJ** protein or its homologs. A vaccine including these peptides, or a vector vaccine encoding them may be used. Alternatively, IgA antibodies to the peptides can be used, preferably as Fab fragments, to induce tolerance. Methods of identifying individuals susceptible to, or at risk for, developing **rheumatoid arthritis** are also described. **DnaJ** of Escherichia coli was found to induce cellular proliferation in peripheral blood lymphocytes of early stage **rheumatoid arthritis**.

L18 ANSWER 10 OF 35 SCISEARCH COPYRIGHT 2003 THOMSON ISI

ACCESSION NUMBER: 97:848074 SCISEARCH
THE GENUINE ARTICLE: XY634
TITLE: Isolation and characterization of an IgG monoclonal anti-**dnaJ** antibody from a patient with **rheumatoid arthritis.**
AUTHOR: Chukwuocha R U (Reprint); Zhang B P; Lai C J; Scavulli J F; **Albani S; Carson D A** ; Chen P J P
CORPORATE SOURCE: UNIV CALIF SAN DIEGO, DEPT MED, LA JOLLA, CA 92093; UNIV CALIF SAN DIEGO, SAM & ROSE STEIN INST RES AGING, LA JOLLA, CA 92093; KAISER PERMANENTE, SAN DIEGO, CA 92123
COUNTRY OF AUTHOR: USA
SOURCE: ARTHRITIS AND RHEUMATISM, (SEP 1997) Vol. 40, No. 9, Supp. [S], pp. 1334-1334.
Publisher: LIPPINCOTT-RAVEN PUBL, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0004-3591.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 0

L18 ANSWER 11 OF 35 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 97:847741 SCISEARCH
THE GENUINE ARTICLE: XY634
TITLE: Production of proinflammatory cytokines by T cells from **rheumatoid arthritis** (**RA**) patients reactive to ''shared epitope'' peptides on the **dnaJ** heat shock protein.
AUTHOR: Samodal R (Reprint); Amox D; Yang X N; Louie S; deKleer I; Vu A; Samodal G; Bonnin D; **Carson D A; Albani S**
CORPORATE SOURCE: UNIV CALIF SAN DIEGO, LA JOLLA, CA 92093
COUNTRY OF AUTHOR: USA
SOURCE: ARTHRITIS AND RHEUMATISM, (SEP 1997) Vol. 40, No. 9, Supp. [S], pp. 1000-1000.
Publisher: LIPPINCOTT-RAVEN PUBL, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0004-3591.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 0

L18 ANSWER 12 OF 35 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 97:607972 SCISEARCH
THE GENUINE ARTICLE: XQ280
TITLE: Genetic bias in immune responses to a cassette shared by different microorganisms in patients with **rheumatoid arthritis**
AUTHOR: LaCava A (Reprint); Nelson J L; Ollier W E R; MacGregor A; Keystone E C; Thorne J C; Scavulli J F; Berry C C; **Carson D A; Albani S**
CORPORATE SOURCE: UNIV CALIF SAN DIEGO, DEPT MED, 9500 GILMAN DR, LA JOLLA, CA 92093 (Reprint); UNIV CALIF SAN DIEGO, DEPT PEDIAT, LA JOLLA, CA 92093; UNIV CALIF SAN DIEGO, SAM & ROSE STEIN INST RES AGING, LA JOLLA, CA

92093; UNIV CALIF SAN DIEGO, DEPT FAMILY & PREVENT MED, LA JOLLA, CA 92093; FRED HUTCHINSON CANC RES CTR, DIV IMMUNOGENET, SEATTLE, WA 98104; UNIV MANCHESTER, ARC, EPIDEMIOL RES UNIT, MANCHESTER M13 9PT, LANCS, ENGLAND; ST THOMAS HOSP, TWIN RES UNIT, LONDON, ENGLAND; WELLESLEY HOSP, RHEUMAT DIS UNIT, TORONTO, ON M4Y 1J3, CANADA; KAISER PERMANENTE HOSP, SAN DIEGO, CA 92120
COUNTRY OF AUTHOR: USA; ENGLAND; CANADA
SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (1 AUG 1997) Vol. 100, No. 3, pp. 658-663.
Publisher: ROCKEFELLER UNIV PRESS, 1114 FIRST AVE, 4TH FL, NEW YORK, NY 10021.
ISSN: 0021-9738.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 23
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **Rheumatoid arthritis** (**RA**) is an autoimmune disease associated with HLA-DR beta 1 alleles which contain the QKRAA amino acid sequence in their third hypervariable region(s), The QKRAA sequence is also expressed by several human pathogens, We have shown previously that an Escherichia coli peptide encompassing QKRAA is a target of immune responses in **RA** patients, Here we address two questions: first, whether QKRAA may function as an ''immunological cassette'' with similar, **RA** -associated, immunogenic properties when expressed by other common human pathogens; and second, what is the influence of genetic background in the generation of these responses, We find that early **RA** patients have enhanced humoral and cellular immune responses to Epstein-Barr virus and Brucella ovis and Lactobacillus lactis antigens which contain the QKRAA sequence, These results suggest that the QKRAA sequence is an antigenic epitope on several different microbial proteins, and that **RA** patients recognize the immunological cassette on different backgrounds, ANOVA of immune responses to ''shared epitope'' antigens in monozygotic twin couples shows that, despite significantly elevated responses in affected individuals, a similarity between pairs is retained, thus suggesting a role played either by hereditary or shared environmental factors in the genesis or maintenance of these responses.

L18 ANSWER 13 OF 35 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:158261 BIOSIS
DOCUMENT NUMBER: PREV199800158261
TITLE: Isolation and characterization of an IgG monoclonal anti-**dnaJ** antibody from a patient with **rheumatoid arthritis.**
AUTHOR(S): Chukwuocha, Reginald U. (1); Zhang, Baoping (1); Lai, Chung-Jeng (1); Scavulli, John F.; **Albani, Salvatore (1); Carson, Dennis A. (1);** Chen, Pojen P. (1)
CORPORATE SOURCE: (1) Dep. Med., Calif. San Diego, La Jolla, CA 92093 USA
SOURCE: Arthritis & Rheumatism, (Sept., 1997) Vol. 40, No. 9 SUPPL., pp. S253.
Meeting Info.: 61st National Scientific Meeting of

the American College of Rheumatology and the 32nd National Scientific Meeting of the Association of Rheumatology Health Professionals Washington, DC, USA November 8-12, 1997 Association of Rheumatology Health Professionals
. ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L18 ANSWER 14 OF 35 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:157928 BIOSIS
DOCUMENT NUMBER: PREV199800157928
TITLE: Production of proinflammatory cytokines by T cells from **rheumatoid arthritis** (**RA**) patients reactive to "shared epitode" peptides on the **dnaJ** heart shock protein.
AUTHOR(S): Samodal, Rodrigo; Amox, Diane; Yang, Xinia; Louie, Stephen; De Kleer, Isme; Vu, An; Samodal, Grace; Bonnin, Dustan; **Carson, Dennis A.**; **Albani, Salvatore**
CORPORATE SOURCE: UCSD, La Jolla, CA 92093 USA
SOURCE: Arthritis & Rheumatism, (Sept., 1997) Vol. 40, No. 9 SUPPL., pp. S197.
Meeting Info.: 61st National Scientific Meeting of the American College of Rheumatology and the 32nd National Scientific Meeting of the Association of Rheumatology Health Professionals Washington, DC, USA November 8-12, 1997 Association of Rheumatology Health Professionals
. ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L18 ANSWER 15 OF 35 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:625975 HCAPLUS
DOCUMENT NUMBER: 125:272836
TITLE: A multistep molecular mimicry hypothesis for the pathogenesis of **rheumatoid arthritis**
AUTHOR(S): **Albani, Salvatore; Carson, Dennis A.**
CORPORATE SOURCE: Dep. Pediatrics, Univ. California, San Diego, La Jolla, CA, 92093-0663, USA
SOURCE: Immunology Today (1996), 17(10), 466-470
CODEN: IMTOD8; ISSN: 0167-4919
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 52 refs. Pos. selected T cells might be involved in physiol. immune responses to exogenous antigens as well as in abnormal processes leading to autoimmune disease. Here, the authors discuss this notion in the context of a multistep mol. mimicry hypothesis for the etiopathogenesis of **rheumatoid arthritis**, based on the shared epitope, a peptide sequence that is shared by virtually all the HLA alleles correlated to the disease.

L18 ANSWER 16 OF 35 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1996:501404 BIOSIS
DOCUMENT NUMBER: PREV199699223760
TITLE: MHC-derived peptides drive positive T cell selection in the thymus: From a physiological system to an HLA DRB1*0401 transgenic mouse model for **rheumatoid arthritis.**
AUTHOR(S): Bonnin, D. (1); Wamatz, K.; **Carson, D.**; **Albani, S.**
CORPORATE SOURCE: (1) Dep. Med., Univ. California, San Diego, La Jolla, CA 92093 USA
SOURCE: Arthritis & Rheumatism, (1996) Vol. 39, No. 9 SUPPL., pp. S160.
Meeting Info.: 60th National Scientific Meeting of the American College of Rheumatology and the 31st National Scientific Meeting of the Association of Rheumatology Health Professionals Orlando, Florida, USA October 18-22, 1996
ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L18 ANSWER 17 OF 35 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 3
ACCESSION NUMBER: 1996:113371 HCAPLUS
DOCUMENT NUMBER: 124:173427
TITLE: **Arthritogenic** intestinal flora replacement and method and vaccines for the treatment of **rheumatoid arthritis**
INVENTOR(S): **Carson, Dennis A.**; Salvatore, Albani
PATENT ASSIGNEE(S): Reagents of the University of California, USA
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9531984	A1	19951130	WO 1995-US4896	19950424
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9523600	A1	19951218	AU 1995-23600	19950424
AU 696646	B2	19980917		
EP 762881	A1	19970319	EP 1995-917611	19950424
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
HU 76359	A2	19970828	HU 1996-3214	19950424
HU 220101	B	20011028		
JP 10500679	T2	19980120	JP 1995-530288	19950424
NZ 284914	A	20000825	NZ 1995-284914	19950424
FI 9604604	A	19970115	FI 1996-4604	19961118
NO 9604910	A	19961119	NO 1996-4910	19961119

PRIORITY APPLN. INFO.: US 1994-246988 A 19940520
WO 1995-US4896 W 19950424

AB Methods useful in the treatment or prevention of **rheumatoid arthritis** (**RA**) are disclosed. Each method is useful in limiting the exposure of the systemic immune system of a human to **RA arthritogenic** peptides present in the person's gastrointestinal (GI) tract. To this end, one method of the invention reduces the population of **arthritogenic** peptide-producing bacteria in the GI tract (e.g., by means of antibiotics) then replaces those bacteria with ones incapable of producing the **arthritogenic** peptides (e.g., bacteria altered by site-directed mutagenesis to express heat-shock protein **dnaJ** contg. the motif DERAAYDQYGHAAFE instead of QKRAAYDQYGHAAFE). Methods for both passive and active immunization of a human against **arthritogenic** peptides are disclosed, as in a method for identifying persons who are predisposed to develop **RA**.

L18 ANSWER 18 OF 35 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 95:735634 SCISEARCH
THE GENUINE ARTICLE: RX684
TITLE: A HUMAN PROTEIN IS THE ULTIMATE TARGET OF ABNORMAL IMMUNE-RESPONSES TO THE ESCHERICHIA-COLI HEAT-SHOCK PROTEIN **DNAJ** IN JUVENILE **RHEUMATOID-ARTHRITIS** (JRA)
AUTHOR: **ALBANI S (Reprint)**; MONTEMAYOR A C; LACAVA A; **CARSON D A**
CORPORATE SOURCE: UNIV CALIF SAN DIEGO, LA JOLLA, CA, 92093; UNIV PAVIA, I-27100 PAVIA, ITALY
COUNTRY OF AUTHOR: USA; ITALY
SOURCE: ARTHRITIS AND RHEUMATISM, (SEP 1995) Vol. 38, No. 9, Supp. S, pp. 933.
ISSN: 0004-3591.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: No References

L18 ANSWER 19 OF 35 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 4
ACCESSION NUMBER: 1995:560363 HCAPLUS
DOCUMENT NUMBER: 122:312551
TITLE: Positive selection in autoimmunity: Abnormal immune responses to a bacterial **dnaJ** antigenic determinant in patients with early **rheumatoid arthritis**
AUTHOR(S): **Albani, Salvatore**; Keystone, Edward C.; Nelson, J. Lee; Ollier, William E. R.; La Cava, Antonio; Montemayor, Ann C.; Weber, Deborah A.; Montecucco, Carlomaurizio; Martini, Alberto; et al.
CORPORATE SOURCE: Sand and Rose Stein Institute Research on Aging, University California, La Jolla, CA, 92093-0663, USA
SOURCE: Nature Medicine (New York) (1995), 1(5), 448-52
CODEN: NAMEFI; ISSN: 1078-8956
PUBLISHER: Nature Publishing Co.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A novel multistep mimicry mechanism for induction of **rheumatoid arthritis** (**RA**) by bacterial antigens that activate T lymphocytes previously educated by peptides derived from a class of human histocompatibility antigens is reported here. These antigens have the amino acid sequence QKRAA, which is also present on the Escherichia coli heat-shock protein **dnaJ**. Synovial fluid cells of early RA patients have strong immune responses to the bacterial antigen, but cells from normal subjects or controls with other autoimmune diseases do not. The activated T cells may cross-react with autologous **dnaJ** heat-shock proteins that are expressed at synovial sites of inflammation. Our findings may have direct relevance to new strategies for the immune therapy of RA.

L18 ANSWER 20 OF 35 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:521440 BIOSIS
DOCUMENT NUMBER: PREV199598535740
TITLE: A human protein is the ultimate target of abnormal immune responses to the E. coli heat shock protein **dnaJ** in juvenile **rheumatoid arthritis** (JRA.
AUTHOR(S): **Albani, Salvatore**; Montemayor, Ann C.; La Cava, Antonio; **Carson, Dennis A. (1)**; Massa, Margherita; Ravelli, Angelo; Debenedetti, Fabrizio; Martini, Alberto
CORPORATE SOURCE: (1) Univ. Pavia, Pavia Italy
SOURCE: Arthritis & Rheumatism, (1995) Vol. 38, No. 9 SUPPL., pp. S308.
Meeting Info.: 59th National Scientific Meeting of the American College of Rheumatology and the 30th National Scientific Meeting of the Association of Rheumatology Health Professionals San Francisco, California, USA October 21-26, 1995
ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L18 ANSWER 21 OF 35 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 94201959 MEDLINE
DOCUMENT NUMBER: 94201959 PubMed ID: 8151470
TITLE: Immune responses to the Escherichia coli **dnaJ** heat shock protein in juvenile **rheumatoid arthritis** and their correlation with disease activity.
AUTHOR: **Albani S**; Ravelli A; Massa M; De Benedetti F; Andree G; Roudier J; Martini A; **Carson D A**
CORPORATE SOURCE: Department of Medicine, University of California, San Diego 92093-0663.
CONTRACT NUMBER: AR25443 (NIAMS)
AR40770 (NIAMS)
SOURCE: JOURNAL OF PEDIATRICS, (1994 Apr) 124 (4) 561-5.
Journal code: 0375410. ISSN: 0022-3476.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199405
ENTRY DATE: Entered STN: 19940523

Last Updated on STN: 19940523
Entered Medline: 19940510

AB Patients with juvenile **rheumatoid arthritis** frequently have abnormal immune responses to the hsp65 class of bacterial heat shock proteins. However, lymphocytes from children with other inflammatory diseases may also recognize hsp65, and the role of these antigens in juvenile **rheumatoid arthritis** remains controversial. We have studied humoral and cellular immune responses to a distinct, recently described bacterial heat shock protein, designated **dnaJ**. The Escherichia coli **dnaJ** gene was cloned and expressed, and the purified recombinant protein was used as an antigen. Neither normal children nor children with various chronic inflammatory diseases had lymphocyte proliferative responses to recombinant **dnaJ**. However, lymphocytes from patients with polyarticular, pauciarticular, and systemic manifestations of juvenile **rheumatoid arthritis** responded strongly to the antigen. Cellular immune responses to **dnaJ** were higher in synovial fluid than in blood and higher in children with active disease than in children in remission. These data show that increased immune reactivity to **dnaJ** is characteristic of juvenile **rheumatoid arthritis** and that the magnitude of the immune response is linked to disease activity. The results suggest that an abnormal immune response to antigens on commensal gut bacteria may contribute to the generation of chronic inflammation in juvenile **rheumatoid arthritis**.

L18 ANSWER 22 OF 35 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:3704 BIOSIS
DOCUMENT NUMBER: PREV199598018004
TITLE: Characterization in enteric bacteria of equivalents of E. coli **dnaJ**, a protein that shares with several HLA alleles the QKRAA susceptibility sequence to **rheumatoid arthritis** (**RA.**
AUTHOR(S): **Albani, Salvatore**; La Cava, Antonio; Schrauder, Andre; **Carson, Dennis A.**
CORPORATE SOURCE: Univ. Calif. San Diego, La Jolla, CA 92093-0663 USA
SOURCE: Arthritis & Rheumatism, (1994) Vol. 37, No. 9 SUPPL., pp. S169.
Meeting Info.: 58th National Scientific Meeting of the American College of Rheumatology and the 29th National Scientific Meeting of the Association of Rheumatology Health Professionals Minneapolis, Minnesota, USA October 23-27, 1994
ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L18 ANSWER 23 OF 35 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 94:512813 SCISEARCH
THE GENUINE ARTICLE: PB897
TITLE: INFECTION AND MOLECULAR MIMICRY IN AUTOIMMUNE-DISEASES OF CHILDHOOD
AUTHOR: **ALBANI S (Reprint)**
CORPORATE SOURCE: UNIV CALIF SAN DIEGO, DEPT PEDIAT, 9500 GILMAN DR, LA JOLLA, CA, 92093 (Reprint); UNIV PAVIA, DEPT PEDIAT, I-27100 PAVIA, ITALY

COUNTRY OF AUTHOR: USA; ITALY
SOURCE: CLINICAL AND EXPERIMENTAL RHEUMATOLOGY, (SEP/OCT 1994) Vol. 12, Supp. 10, pp. S35-S41.
ISSN: 0392-856X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: 35

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The etiopathogenesis of childhood chronic autoimmune disease is, in most cases, unknown. Most likely, several factors overlap in determining the loss of tolerance toward certain autoantigens that become the target of the disease and the main cause of its perpetuation. Infectious agents have often been implicated in the pathogenesis of these diseases, but, to date, compelling evidence for a horizontal transmission or for localized epidemics is lacking. Human pathogens may never the less play a role in determining the loss of tolerance toward certain self-antigens by means of mechanisms other than classic infection. It is common knowledge that human pathogens often express proteins with high antigenic potential with important homologies with human proteins. Evolutionary pressures based upon the necessity of escaping the host's specific immune responses may have determined this phenomenon, called ''molecular mimicry''.

It is reasonable to assert that certain individuals can develop abnormal immune responses upon contact with an antigen that mimics a self-protein. These responses may ultimately lead to self-reactivity and autoimmune disease. In this model of molecular mimicry, self-reactivity is triggered by cross-recognition of a self and an exogenous protein that bear the same sequence. A disease triggered by such a mechanism should present with: i) some form of an acute or chronic autoimmune clinical manifestation; ii) o documented clinical correlation between contact with a human pathogen and the autoimmune disease; iii) immune cross-reaction between a protein from a pathogen and a homologous human protein.

Acute rheumatic fever, Reiter's syndrome and the other reactive arthritides fulfill the above conditions. Our hypothesis is that similar mechanisms may contribute to the pathogenesis of other autoimmune diseases in childhood I will discuss herein our work on juvenile **rheumatoid arthritis** and juvenile dermatomyositis.

L18 ANSWER 24 OF 35 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1994:9416 BIOSIS
DOCUMENT NUMBER: PREV199497022416

TITLE: The QKRAA disease susceptibility sequence for **rheumatoid arthritis** (**RA**) is a B cell epitope shared by the Epstein-Barr virus (EBV) protein gp110 and the E. coli heat shock protein **dnaJ**. Possible implications for disease pathogenesis.

AUTHOR(S): La Cava, A. (1); Andree, G. (1); Roudier, J.; **Carson, D. (1); Albani, S. (1)**
CORPORATE SOURCE: (1) UCLA, La Jolla, CA 92093-0663 USA

SOURCE: Arthritis and Rheumatism, (1993) Vol. 36, No. 9 SUPPL., pp. S127.
Meeting Info.: 57th Annual Scientific Meeting of the American College of Rheumatology San Antonio, Texas,

USA November 7-11, 1993
ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L18 ANSWER 25 OF 35 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 93:639760 SCISEARCH
THE GENUINE ARTICLE: MB816
TITLE: THE QKRAA DISEASE SUSCEPTIBILITY SEQUENCE FOR **RHEUMATOID-ARTHRITIS** (**RA**) IS A B-CELL EPITOPE SHARED BY THE EPSTEIN-BARR-VIRUS (EBV) PROTEIN GP110 AND THE ESCHERICHIA-COLI HEAT-SHOCK PROTEIN **DNAJ** POSSIBLE IMPLICATIONS FOR DISEASE PATHOGENESIS
AUTHOR: LACAVA A (Reprint); ANDREE G; ROUDIER J; **CARSON D; ALBANI S**
CORPORATE SOURCE: UCSD, LA JOLLA, CA, 92093; UNIV AIX MARSEILLE 2, F-13007 MARSEILLE, FRANCE
COUNTRY OF AUTHOR: USA; FRANCE
SOURCE: ARTHRITIS AND RHEUMATISM, (SEP 1993) Vol. 36, No. 9, Supp. S, pp. S127.
ISSN: 0004-3591.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: No References

L18 ANSWER 26 OF 35 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1994:8986 BIOSIS
DOCUMENT NUMBER: PREV199497021986
TITLE: The HLA DR4 Dw4 susceptibility sequence to **rheumatoid arthritis**, as expressed on the E. coli heat shock protein **dnaJ**, is a target of T and B cell responses in patients with **RA**.
AUTHOR(S): **Albani, S. (1)**; Keystone, E.; Ollier, W.; Montecucco, C.; Caporali, R.; Massa, M.; Martini, A.; Roudier, J.; **Carson, D.**
CORPORATE SOURCE: (1) Univ. Calif. San Diego, La Jolla, CA 92093-0663 USA
SOURCE: Arthritis and Rheumatism, (1993) Vol. 36, No. 9 SUPPL., pp. S55.
Meeting Info.: 57th Annual Scientific Meeting of the American College of Rheumatology San Antonio, Texas, USA November 7-11, 1993
ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L18 ANSWER 27 OF 35 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 93:639330 SCISEARCH
THE GENUINE ARTICLE: MB816
TITLE: THE HLA DR4 DW4 SUSCEPTIBILITY SEQUENCE TO **RHEUMATOID-ARTHRITIS**, AS EXPRESSED ON THE ESCHERICHIA-COLI HEAT-SHOCK PROTEIN **DNAJ**, IS A TARGET OF T-CELL AND B-CELL RESPONSES IN PATIENTS WITH **RA**
AUTHOR: **ALBANI S (Reprint)**; KEYSTONE E; OLLIER W;

MONTECUCCO C; CAPORALI R; MASSA M; MARTINI A; ROUDIER J; **CARSON D**
CORPORATE SOURCE: UNIV CALIF SAN DIEGO, LA JOLLA, CA, 92093; UNIV MARSEILLE, MARSEILLE, FRANCE; UNIV TORONTO, TORONTO M5S 1A1, ONTARIO, CANADA; UNIV MANCHESTER, MANCHESTER M13 9PL, LANCS, ENGLAND; UNIV PAVIA, I-27100 PAVIA, ITALY
COUNTRY OF AUTHOR: USA; FRANCE; CANADA; ENGLAND; ITALY
SOURCE: ARTHRITIS AND RHEUMATISM, (SEP 1993) Vol. 36, No. 9, Supp. S, pp. S55.
ISSN: 0004-3591.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: No References

L18 ANSWER 28 OF 35 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 93087815 MEDLINE
DOCUMENT NUMBER: 93087815 PubMed ID: 1280844
TITLE: Genetic and environmental factors in the immune pathogenesis of **rheumatoid arthritis.**
AUTHOR: **Albani S; Carson D A;** Roudier J
CORPORATE SOURCE: Department of Medicine, University of California, San Diego, La Jolla.
CONTRACT NUMBER: AR07567 (NIAMS)
AR25443 (NIAMS)
AR40770 (NIAMS)
SOURCE: RHEUMATIC DISEASES CLINICS OF NORTH AMERICA, (1992 Nov) 18 (4) 729-40. Ref: 15
Journal code: 8708093. ISSN: 0889-857X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199301
ENTRY DATE: Entered STN: 19930129
Last Updated on STN: 19960129
Entered Medline: 19930104

AB Our experiments have led us to conclude that the **rheumatoid arthritis** shared epitope may act as a peptide that is important for positive and negative selection of T lymphocytes, that T lymphocytes are skewed by positive selection to recognize epitopes that are similar but not identical to self, and that peptide sequences that are similar to the **RA**-shared epitope are abundantly expressed by microorganisms that chronically infect most people. This combination of events could partly explain the association of the shared epitope with the severe forms of RA. The hypothesis cannot be tested directly, because we do not postulate that any unique population of autoreactive T cells is expanded in RA; however, the role of positive selection in molding the human T-cell repertoire to exogenous antigens can be tested by mapping T-cell antigenic determinants on the E. coli **dnaJ** protein or the gp110 protein of EBV in people with different HLA-DR types. Moreover, positive selection models imply that maternal antigens that cross the placenta can influence the T-cell repertoire. Thus,

one might expect to find that the frequency of HLA-DR4 in the mothers of patients with RA who themselves lack the DR4 antigen, would be more frequent than predicted by chance alone. As the principles of positive selection are more precisely delineated in animal systems, it should become possible to ascertain more clearly how the shared epitope on HLA-DR molecules enhances the severity of autoimmune reactions; however, RA only occurs in humans; possibly because of the unique inability of human macrophages to replicate. Thus, only the direct analysis of patients can directly reveal the mechanisms of disease pathogenesis.

L18 ANSWER 29 OF 35 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 7
ACCESSION NUMBER: 1992:57226 HCAPLUS
DOCUMENT NUMBER: 116:57226
TITLE: The susceptibility sequence to **rheumatoid arthritis** is a cross-reactive B cell epitope shared by the Escherichia coli heat shock protein **dnaJ** and the histocompatibility leukocyte antigen DRB10401 molecule
AUTHOR(S): **Albani, Salvatore**; Tuckwell, Julia E.; Esparza, Lucia; **Carson, Dennis A.**; Roudier, Jean
CORPORATE SOURCE: Sam and Rose Stein Inst. Res. Aging, Univ. California, San Diego, La Jolla, CA, 92093-0945, USA
SOURCE: Journal of Clinical Investigation (1992), 89(1), 327-31
CODEN: JCINAO; ISSN: 0021-9738
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Immunol. responses to bacterial heat shock proteins have been implicated in the pathogenesis of arthritis in animals and humans. The predicted amino acid sequence of **dnaJ**, a heat shock protein from E. coli, contains an 11-amino acid segment that is homologous to the third hypervariable region of the human histocompatibility antigen (HLA) DRB10401 (formerly known as HLA Dw4), the part of the mol. that carries susceptibility to **rheumatoid arthritis**. To test the biol. significance of this finding, the authors expressed and purified recombinant **dnaJ** (rdnaJ), and detd. its immunol. cross-reactivity with HLA DRB10401. A rabbit antipeptide antiserum raised against the sequence of the third hypervariable region of HLA DRB10410 specifically bound to rdnaJ, thus confirming that a similar sequence is expressed on the bacterial protein. Of greater consequence, an antiserum to the rdnaJ protein recognized not only a peptide from the third hypervariable region of HLA DRB10401, but also the intact HLA DRB10401 polypeptide. Furthermore, the antibody to rdnaJ reacted with HLA DRB10401 homozygous B lymphoblasts, but not with HLA DRB11501, DRB10101, DRB10301, and DRB10701 (formerly known as HLA Dw2, DR 1, DR 3, and DR 7, in the same order) homozygous cells. Thus, exposure to a bacterial heat shock protein can elicit antibodies against the **rheumatoid arthritis** susceptibility sequence in the third hypervariable region of HLA DRB10401.

L18 ANSWER 30 OF 35 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 8
ACCESSION NUMBER: 1992:549144 HCAPLUS

DOCUMENT NUMBER: 117:149144
TITLE: Molecular basis for the association between HLA DR4 and **rheumatoid arthritis** . From the shared epitope hypothesis to a peptidic model of **rheumatoid arthritis**
AUTHOR(S): **Albani, Salvatore**; Roudier, Jean
CORPORATE SOURCE: Inst. Aging, Univ. California, San Diego, La Jolla, CA, 92037, USA
SOURCE: Clinical Biochemistry (1992), 25(3), 209-12
CODEN: CLBIAS; ISSN: 0009-9120
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Susceptibility to **rheumatoid arthritis** (**RA**) maps to residues QKRAA/QRRAA in the 3rd hypervariable region of the HLA DR.beta.1 chain. Peptides from the same area of MHC class II mols. are able to modulate the T-cell repertoire by deleting self-reactive T-cells. The Epstein Barr virus glycoprotein gp110 and the **DNA J** heat-shock protein from Escherichia coli mimic the 3rd hypervariable region of HLA-Dw4DR.beta.1. Thus, the same area of HLA DR.beta.1 carries susceptibility to RA, modulates the T-cell repertoire, and is mimicked by human pathogens. RA may originate from a particular shape imposed on the T-cell repertoire by the QKRAA/QRRAA sequence in the 3rd hypervariable region of HLA DR.beta.1.

L18 ANSWER 31 OF 35 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1993:18694 BIOSIS
DOCUMENT NUMBER: PREV199344006894
TITLE: Immune response to the Escherichia coli **dnaJ** heat shock protein correlates with disease activity in juvenile **rheumatoid arthritis.**
AUTHOR(S): **Albani, Salvatore (1)**; Ravelli, Angelo; Massa, Margherita; De Benedetti, Fabrizio; Andree, Gregor (1); Roudier, Jean; Martini, Alberto; **Carson, Dennis A. (1)**
CORPORATE SOURCE: (1) Univ. Calif. San Diego, La Jolla, Calif. 92093-0663
SOURCE: Arthritis & Rheumatism, (1992) Vol. 35, No. 9 SUPPL., pp. S56.
Meeting Info.: 56th Annual Scientific Meeting of the American College of Rheumatology, Atlanta, Georgia, USA, October 11-15, 1992. ARTHRITIS RHEUM ISSN: 0004-3591.
DOCUMENT TYPE: Conference
LANGUAGE: English

L18 ANSWER 32 OF 35 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 92:606647 SCISEARCH
THE GENUINE ARTICLE: JR158
TITLE: IMMUNE-RESPONSE TO THE ESCHERICHIA-COLI **DNAJ** HEAT-SHOCK PROTEIN CORRELATES WITH DISEASE-ACTIVITY IN JUVENILE **RHEUMATOID-ARTHRITIS**
AUTHOR: **ALBANI S (Reprint)**; RAVELLI A; MASSA M; DEBENEDETTI F; ANDREE G; ROUDIER J; MARTINI A; **CARSON D A**
CORPORATE SOURCE: UNIV MARSEILLE, MARSEILLE, FRANCE; UNIV CALIF SAN DIEGO, LA JOLLA, CA, 92093; UNIV PAVIA, IRCCS SAN

MATTEO, DEPT PEDIAT, I-27100 PAVIA, ITALY
COUNTRY OF AUTHOR: FRANCE; USA; ITALY
SOURCE: ARTHRITIS AND RHEUMATISM, (SEP 1992) Vol. 35, No. 9, Supp. S, pp. S56.
ISSN: 0004-3591.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: No References

L18 ANSWER 33 OF 35 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1992:19155 BIOSIS
DOCUMENT NUMBER: BR42:6855
TITLE: IMMUNOLOGICAL MATURATION AND DISEASE STATUS IN DIFFUSE CONNECTIVE TISSUE DISEASES AFFECT SERUM REACTIVITY TO A BACTERIAL HEAT SHOCK PROTEIN **DNAJ** THAT IS HOMOLOGOUS TO HLA DW4.
AUTHOR(S): **ALBANI S**; RAVELLI A; MASSA M; **CARSON D A**; MARTINI A; ROUDIER J
CORPORATE SOURCE: UNIV. CALIF., SAN DIEGO, LA JOLLA, CALIF. 92093-0945, USA.
SOURCE: 55TH ANNUAL MEETING OF THE AMERICAN COLLEGE OF RHEUMATOLOGY, BOSTON, MASSACHUSETTS, USA, NOVEMBER 17-21, 1991. ARTHRITIS RHEUM, (1991) 34 (9 SUPPL), S151.
CODEN: ARHEAW. ISSN: 0004-3591.
DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English

L18 ANSWER 34 OF 35 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1992:18513 BIOSIS
DOCUMENT NUMBER: BR42:6213
TITLE: THE **DNAJ** HEAT SHOCK PROTEIN FROM ESCHERICHIA-COLI CROSS REACTS WITH HLA DW4.
AUTHOR(S): **ALBANI S**; **CARSON D A**; ROUDIER J
CORPORATE SOURCE: UNIV. CALIF. SAN DIEGO, LA JOLLA, CALIF. 92093-0945.
SOURCE: 55TH ANNUAL MEETING OF THE AMERICAN COLLEGE OF RHEUMATOLOGY, BOSTON, MASSACHUSETTS, USA, NOVEMBER 17-21, 1991. ARTHRITIS RHEUM, (1991) 34 (9 SUPPL), S41.
CODEN: ARHEAW. ISSN: 0004-3591.
DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English

L18 ANSWER 35 OF 35 CONFSCI COPYRIGHT 2003 CSA
ACCESSION NUMBER: 93:28920 CONFSCI
DOCUMENT NUMBER: 93028920
TITLE: Immune response to the E. coli **dnaJ** heat shock protein correlates with disease activity in juvenile **rheumatoid arthritis**
AUTHOR: **Albani, S.**; Ravelli, A.; Massa, M.; de Benedetti, F; Andree, G.; Roudier, J.
CORPORATE SOURCE: Univ. California at San Diego, La Jolla, CA
SOURCE: ACR, Paper No. 130.
Meeting Info.: 924 5014: 56th Annual Scientific Meeting of the American College of Rheumatology

(9245014). Atlanta, GA (USA). 11-15 Oct 1992.
American College of Rheumatology.
DOCUMENT TYPE: Conference
FILE SEGMENT: DCCP
LANGUAGE: UNAVAILABLE

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FILE 'HOME' ENTERED AT 10:41:06 ON 10 JUL 2003

Shahnan-Shah
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     FILE 'REGISTRY' ENTERED AT 10:28:19 ON 10 JUL 2003
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                E "TRANSFORMING GROWTH FACTOR-.BETA."/CN 5
L1            1 S E4
                E "TRANSFORMING GROWTH FACTOR, BETA"/CN 5
L2            4 S "TRANSFORMING GROWTH FACTOR, BETA"?/CN
L3            5 S L1 OR L2

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                FACTOR-.BETA. (HUMAN CLONE HP00269)"/CN
L2            4 SEA FILE=REGISTRY ABB=ON  PLU=ON  "TRANSFORMING GROWTH
                FACTOR, BETA"?/CN
L3            5 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 OR L2
L4         1023 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DNAJ? OR DNA(W)(J OR
                JPI OR JP1 OR JP(W)(I OR 1))
L5        41239 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 OR (TGF OR TRANSFORM?
                 GROWTH FACTOR)(2A)(B OR BETA) OR TGFB? OR IMMUNOMODULAT?
                 OR IMMUN? MODULAT?
L6           19 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 AND L5


L4         1023 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DNAJ? OR DNA(W)(J OR
                JPI OR JP1 OR JP(W)(I OR 1))
L7           19 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 AND (RA(S)ARTHRIT?
                OR RHEUMATOID? ARTHRIT? OR ARTHRITOGEN?)


L8           36 L6 OR L7

L8   ANSWER 1 OF 36  HCAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2003:409169  HCAPLUS
DOCUMENT NUMBER:          138:380506
TITLE:                    Genes that are differentially expressed during
                          erythropoiesis and their diagnostic and
                          therapeutic uses
INVENTOR(S):              Brissette, William H.; Neote, Kuldeep S.;
                          Zagouras, Panayiotis; Zenke, Martin; Lemke,
                          Britt; Hacker, Christine
PATENT ASSIGNEE(S):       Pfizer Products Inc., USA; Max-Delbruck-Centre
                          for Molecular Medicine
SOURCE:                   PCT Int. Appl., 285 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ----------------  ----  --------      ---------------  --------
     WO 2003038130      A2   20030508      WO 2002-XA34888  20021031
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
             NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
             TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM,
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AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

WO 2003038130 A2 20030508 WO 2002-US34888 20021031
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-335048P P 20011031
US 2001-335183P P 20011102
WO 2002-US34888 A 20021031

AB The present invention provides mol. targets that regulate erythropoiesis. Groups of genes or their encoded gene products comprise panels of the invention and may be used in therapeutic intervention, therapeutic agent screening, and in diagnostic methods for diseases and/or disorders of erythropoiesis. The panels were discovered using gene expression profiling of erythroid progenitors with Affymetrix HU6800 and HG-U95Av2 chips. Cells from an in vitro growth and differentiation system of SCF-Epo dependent human erythroid progenitors, E-cadherin+/CD36+ progenitors, cord blood, or CD34+ peripheral blood stem cells were analyzed. The HU6800 chip contains probes from 13,000 genes with a potential role in cell growth, proliferation, and differentiation and the HG-U95Av2 chip contains 12,000 full-length, functionally-characterized genes. [This abstr. record is one of two records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.].

L8 ANSWER 2 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:351016 HCAPLUS
DOCUMENT NUMBER: 138:383799
TITLE: Characterization of the anti-**DnaJ** monoclonal antibodies and their use to compare immunological properties of **DnaJ** and its human homologue HDJ-1
AUTHOR(S): Krzewski, Konrad; Kunikowska, Danuta; Wysocki, Jan; Kotlarz, Agnieszka; Thompkins, Philip; Ashraf, William; Lindsey, Nigel; Picksley, Steven; Glosnicka, Renata; Lipinska, Barbara
CORPORATE SOURCE: Department of Biochemistry, University of Gdansk, Pol.
SOURCE: Cell Stress & Chaperones (2003), 8(1), 8-17
CODEN: CSCHFG; ISSN: 1355-8145
PUBLISHER: Cell Stress Society International
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Escherichia coli **DnaJ** (Hsp40) is suspected to participate in **rheumatoid arthritis** (**RA**) pathogenesis in humans by an autoimmune process. In this work a set

of 6 anti-**DnaJ** monoclonal antibodies (mAbs) was raised and localization of the epitopes recognized by the mAbs was investigated. Western blotting and ELISA expts. showed that the mAbs efficiently bound only native antigen. Using **DnaJ** mutant proteins with deletions of specified domains and ELISA, we found that AC11 mAb reacted with the best conserved in evolution N-terminal J domain, whereas BB3, EE11, CC5, CC8, and DC7 bound to the C-terminal part after residue 200. Mapping performed with the use of a random peptide library displayed by filamentous phage indicated that (1) AC11 mAb bound to a region between residues 33-48, including D-34 which belongs to the HPD triad, present in all **DnaJ** homologues, (2) BB3 recognized residues localized in the 204-224 region, (3) EE11 recognized the 291-309 region, (4) CC5-the region 326-359, and (5) CC8-the 346-366 region. All these mAbs, as well as the polyclonal antibodies against the N- or C-terminal domain, bound efficiently to HDJ-1, human Hsp40. These results show the presence of a significant immunol. similarity between bacterial **DnaJ** and human HDJ-1, which is not restricted to the evolutionarily conserved parts of the proteins, and suggest that HDJ-1 could be a possible target of immune response triggered by **DnaJ**.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:301302 HCAPLUS
DOCUMENT NUMBER: 138:314563
TITLE: Cancer-associated genes and methods for diagnosis and treatment of cancer
INVENTOR(S): Vogelstein, Bert; Kinzler, Kenneth W.; Saha, Saurabh; Bardelli, Alberto
PATENT ASSIGNEE(S): The Johns Hopkins University, USA
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003031930	A2	20030417	WO 2002-US31247	20021002

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-327332P P 20011009

AB A method of identifying cancers, and for detecting or predicting metastases, in the body by administering antibodies specific for tumor markers is disclosed. Addnl., antibodies or other substances

binding to these tumor markers may be used to treat cancer. Thus, the global gene expression profile of metastatic colorectal cancer was compared to that of primary cancers, benign colorectal tumors, and normal colorectal epithelium. Among 38 cancer-assocd. genes identified, the protein tyrosine phosphatase gene PRL3/PTP4A3 was of particular interest. It was expressed at high levels in each of 18 cancer metastases studied but at lower levels in non-metastatic tumors and normal colorectal epithelium. In three of twelve metastases examd., multiple copies of the PRL3 gene were found within a small amplicon located at chromosome 8q24.3. These data suggest that the PRL3 gene is important for colorectal cancer metastasis and provides a new therapeutic target for these intractable lesions.

L8 ANSWER 4 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:282589 HCAPLUS
DOCUMENT NUMBER: 138:285610
TITLE: Classification of lung carcinomas by analysis of patterns of gene expression
INVENTOR(S): Golub, Todd; Meyerson, Matthew; Bhattacharjee, Arindham; Staunton, Jane
PATENT ASSIGNEE(S): Whitehead Institute for Biomedical Research, USA
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003029273	A2	20030410	WO 2002-US30797	20020927

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-325962P P 20010928

AB The invention provides a mol. taxonomy of lung carcinoma, the leading cause of cancer death in the United States and worldwide. Oligonucleotide micro arrays were used to analyze mRNA expression levels corresponding to 12,600 transcript sequences in 186 lung tumor samples, including 139 adenocarcinomas resected from the lung. Genes showing high levels of expression in normal lung were identified. Hierarchical and probabilistic clustering of expression data defined distinct subclasses of lung adenocarcinoma. Among these were tumors with high relative expression of neuroendocrine genes and of type II pneumocyte genes, resp. Retrospective anal. revealed a less favorable outcome for the adenocarcinomas with neuroendocrine gene expression. The diagnostic potential of expression profiling is emphasized by its ability to discriminate primary lung adenocarcinomas from metastases of extrapulmonary

origin. These results suggest that integration of expression profile data with clin. parameters could aid in diagnosis of lung cancer patients.

L8 ANSWER 5 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:247387 HCAPLUS
DOCUMENT NUMBER: 139:4586
TITLE: Egr1 Promotes Growth and Survival of Prostate Cancer Cells. Identification of novel Egr1 target genes.
AUTHOR(S): Virolle, Thierry; Krones-Herzig, Anja; Baron, Veronique; De Gregorio, Giorgia; Adamson, Eileen D.; Mercola, Dan
CORPORATE SOURCE: La Jolla Cancer Research Center, The Burnham Institute, La Jolla, CA, 92037, USA
SOURCE: Journal of Biological Chemistry (2003), 278(14), 11802-11810
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the majority of aggressive tumorigenic prostate cancer cells, the transcription factor Egr1 is overexpressed. The authors provide new insights of Egr1 involvement in proliferation and survival of TRAMP C2 prostate cancer cells by the identification of several new target genes controlling growth, cell cycle progression, and apoptosis such as cyclin D2, p19ink4d, and Fas. Egr1 regulation of these genes, identified by Affymetrix microarray, was confirmed by real-time PCR, immunoblot, and chromatin immunopptn. assays. Furthermore the authors also showed that Egr1 is responsible for cyclin D2 overexpression in tumorigenic DU145 human prostate cells. The regulation of these genes by Egr1 was demonstrated using Egr1 antisense oligonucleotides that further implicated Egr1 in resistance to apoptotic signals. One mechanism was illustrated by the ability of Egr1 to inhibit CD95 (Fas/Apo) expression, leading to insensitivity to FasL. The results provide a mechanistic basis for the oncogenic role of Egr1 in TRAMP C2 prostate cancer cells.
REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:242437 HCAPLUS
DOCUMENT NUMBER: 138:249938
TITLE: Gene expression profile biomarkers and therapeutic targets for brain aging and age-related cognitive impairment in rats
INVENTOR(S): Landfield, Philip W.; Blalock, Eric M.; Chen, Kuey-Chu; Foster, Thomas C.
PATENT ASSIGNEE(S): University of Kentucky Research Foundation, USA
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003025122	A2	20030327	WO 2002-US25607	20020813

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-311343P P 20010813

AB A statistical and functional correlation strategy is provided to identify changes in cellular pathways specifically linked to impaired cognitive function with aging. Analyses using the strategy identified multiple groups of genes expressed in the hippocampal CA1 region of rats, where the genes were expressed at different levels for several ages. The aging changes in expression began before mid-life. Many of the genes were involved in specific neuronal and glial pathways with previously unrecognized relationships to aging and/or cognitive decline. The processes identified by the strategy suggest a new hypothesis of brain aging in which initially decreased neuronal activity and/or oxidative metab. trigger sep. but parallel genomic cascades in neurons and glia. In neurons, the cascade results in elevations in calcium signaling and redns. of immediate early gene signaling, biosynthesis, synaptogenesis, and neurite remodeling. In contrast, glia undergo increased lipid metab. and mediate a cycle of demyelination and remyelination that induces antigen presentation, inflammation, oxidative stress, and extracellular restructuring. These identified genes and the proteins they encode can be used as novel biomarkers of brain aging and as targets for developing treatment methods against age-related cognitive decline, Alzheimer's disease, and Parkinson's disease.

L8 ANSWER 7 OF 36 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2003:176884 HCAPLUS
DOCUMENT NUMBER: 138:367082
TITLE: Genome-wide cDNA microarray analysis of gene-expression profiles involved in ovarian endometriosis
AUTHOR(S): Arimoto, Takahide; Katagiri, Toyomasa; Oda, Katsutoshi; Tsunoda, Tatsuhiko; Yasugi, Toshiharu; Osuga, Yutaka; Yoshikawa, Hiroyuki; Nishii, Osamu; Yano, Tetsu; Taketani, Yuji; Nakamura, Yusuke
CORPORATE SOURCE: Laboratory of Molecular Medicine, Human Genome Center, Institute of Medical Science, The University of Tokyo, Minato-ku, Tokyo, 108-8639, Japan
SOURCE: International Journal of Oncology (2003), 22(3), 551-560
CODEN: IJONES; ISSN: 1019-6439
PUBLISHER: International Journal of Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Using a cDNA microarray consisting of 23,040 genes, the authors analyzed gene-expression profiles of ovarian endometrial cysts from 23 patients to identify genes involved in endometriosis. By comparing expression patterns between endometriotic tissues and corresponding eutopic endometria, the authors identified 15 genes that were commonly upregulated in the endometrial cysts during both proliferative and secretory phases of the menstrual cycle, 42 that were upregulated only in the proliferative phase, and 40 that were up-regulated only in the secretory phase. The up-regulated elements included genes encoding some HLA antigens, complement factors, ribosomal proteins, and **TGFBI**. 337 Genes were commonly down-regulated throughout the menstrual cycle, 144 only in the proliferative phase, and 835 only in the secretory phase. The down-regulated elements included the tumor suppressor TP53, genes related to apoptosis such as GADD34, GADD45A, GADD45B and PIG11, and the gene encoding OVGP1, a protein involved in maintenance of early pregnancy. Semi-quant. RT-PCR expts. supported the results of the authors' microarray anal. These data should provide useful information for finding candidate genes whose products might serve as mol. targets for diagnosis or treatment of endometriosis.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:927627 HCAPLUS
DOCUMENT NUMBER: 138:23681
TITLE: Marker genes for the diagnosis, molecular definition and development of treatment of chronic inflammatory joint diseases using microarray technologies
INVENTOR(S): Haeupl, Thomas; Ungethuem, Ute; Blaess, Stefan
PATENT ASSIGNEE(S): Pathoarray GmbH, Germany
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002097125	A2	20021205	WO 2002-DE2010	20020530
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10127572	A1	20021205	DE 2001-10127572	20010530
DE 10225853	A1	20030515	DE 2002-10225853	20020530

PRIORITY APPLN. INFO.: DE 2001-10127572 A 20010530

AB The invention relates to tools for the diagnosis, mol. definition

and development of treatment of chronic inflammatory joint diseases and other inflammatory, infectious or tumorous diseases. According to the invention, genome data (genomics), proteome data (proteomics) and immunome data (immunomics) are used in the anal. and development of treatment of chronic joint diseases. Anal. of patterns of gene expression at the mRNA or protein level and of the distribution of antigens are used to characterize inflammatory and non-inflammatory rheumatic joint diseases, auto-immune diseases and infectious diseases and in the identification of diagnostic indicators. Etiol. significant pathogenic factors in chronic inflammatory joint diseases which have been unclear until now can be derived from the examns. carried out. Furthermore, interpretation algorithms can be created for the classification, prognosis evaluation and treatment optimization of said joint diseases, and new strategies for treatment and points of attack for medicaments can be derived.

L8 ANSWER 9 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:869083 HCAPLUS
DOCUMENT NUMBER: 137:381501
TITLE: Protein-protein interaction domains of adipocyte proteins and method for screening for association-inhibiting drugs
INVENTOR(S): Legrain, Pierre; Whiteside, Simon; Mao, Jen-I.; Khrebtukova, Irina; Luo, Shujun
PATENT ASSIGNEE(S): Hybrigenics, Fr.; Lynx Therapeutics Inc.
SOURCE: PCT Int. Appl., 232 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002090544	A2	20021114	WO 2002-EP6333	20020503

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-288885P P 20010504

AB The present invention relates to protein-protein interactions of adipocytes. More specifically, the present invention relates to complexes of polypeptides, or polynucleotides encoding the polypeptides, interaction domains of the polypeptides, methods for screening drugs which modulate the interaction of proteins, and pharmaceutical compns. that are capable of modulating the protein-protein interactions. Thus, gene expression profiles of differentiated and undifferentiated human PAZ6 cells indicated that genes for the following proteins were overexpressed in the differentiated cells (adipocytes): protein TPT1 (tumor protein, translationally controlled, 1), leptin, complement component 1,

thymosin .beta.4, fibulin 1C, osteonectin, .beta.2-microglobulin, proteasome subunit p31, huntingtin-interacting protein 2, and two interferon-inducible proteins. In a modified yeast two-hybrid system, the protein interaction domains of these proteins were used as bait to identify proteins with which they interact. The DVL1, DVL2, and DVL3 (dishevelled 1, 2 and 3) proteins of the Wnt signaling pathway were all found to interact with the PSMD8 protein, i.e., proteasome subunit p31.

L8 ANSWER 10 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:521969 HCAPLUS
DOCUMENT NUMBER: 137:90000
TITLE: Protein-protein interactions in adipocyte cells and method for selecting modulators of these interactions
INVENTOR(S): Legrain, Pierre; Marullo, Stefano; Jockers, Ralf
PATENT ASSIGNEE(S): Hybrigenics, Fr.; Centre National De La Recherche Scientifique
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053726	A2	20020711	WO 2001-EP15423	20011228
WO 2002053726	A3	20030313		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003040089	A1	20030227	US 2002-38010	20020102

PRIORITY APPLN. INFO.: US 2001-259377P P 20010102
AB The present invention relates to protein-protein interactions of adipocyte. More specifically, the present invention relates to complexes of polypeptides, or polynucleotides encoding the polypeptides, fragments of the polypeptides, antibodies to the complexes. Selected Interacting Domains (SID) which are identified due to the protein-protein interactions, methods for screening drugs for agents which modulate the interaction of proteins, and pharmaceutical compns. that are capable of modulating the protein-protein interactions are further disclosed.

L8 ANSWER 11 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:440862 HCAPLUS
DOCUMENT NUMBER: 137:346973
TITLE: GIPC gene family (review)
AUTHOR(S): Katoh, Masaru
CORPORATE SOURCE: Genetics and Cell Biology Section, Genetics

Division, National Cancer Center Research Institute, Chuo-ku, Tokyo, 104-0045, Japan
SOURCE: International Journal of Molecular Medicine (2002), 9(6), 585-589
CODEN: IJMMFG; ISSN: 1107-3756
PUBLISHER: International Journal of Molecular Medicine
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. GIPC1/GIPC/RGS191P1, GIPC2, and GIPC3 genes constitute the human GIPC gene family. GIPC1 and GIPC2 show 62.0% total-amino-acid identity. GEPC1 and GIPC3 show 59.9% total-amino-acid identity. GIPC2 and GIPC3 show 55.3% total-amino-acid identity. GIPCs are proteins with central PDZ domain and GIPC homol. (GH1 and GH2) domains. PDZ, GH1, and GH2 domains are conserved among human GIPCs, Xenopus GIPC/Kermit, and Drosophila GIPC/LP09416. Bioinformatics revealed that GIPC genes are linked to prostanoid receptor genes and **DNAJB** genes in the human genome as follows: GIPC1 gene is linked to prostaglandin E receptor 1 (PTGER1) gene and **DNAJB1** gene in human chromosome 19p13.2-p13.1 region; GIPC2 gene to prostaglandin F receptor (PTGFR) gene and **DNAJB4** gene in human chromosome 1p31.1-p22.3 region; GIPC3 gene to thromboxane A2 receptor (TBXA2R) gene in human chromosome 19p13.3 region. GIPC1 and GIPC2 mRNAs are expressed together in OKAJIMA, TMK1, MKN45 and KATO-III cells derived from diffuse-type of gastric cancer, and are up-regulated in several cases of primary gastric cancer. PDZ domain of GIPC family proteins interact with Frizzled-3 (FZD3) class of WNT receptor, insulin-like growth factor-I (IGF1) receptor, receptor tyrosine kinase TrkA, **TGF-.beta.** type III receptor (**TGF-.beta.** RIII), integrin .alpha.6A subunit, transmembrane glycoprotein 5T4, and RGS 19/RGS-GAIP. Because RGS19 is a member of the RGS family that regulate heterotrimeric G-protein signaling, GIPCs might be scaffold proteins linking heterotrimeric G-proteins to seven-transmembrane-type WNT receptor or to receptor tyrosine kinases. Therefore, GIPC1, GIPC2 and GIPC3 might play key roles in carcinogenesis and embryogenesis through modulation of growth factor signaling and cell adhesion.

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:369654 HCAPLUS
DOCUMENT NUMBER: 137:246375
TITLE: Interaction between heat-shock protein 73 and HLA-DRB1 alleles associated or not with **rheumatoid arthritis**
AUTHOR(S): Auger, Isabelle; Lepecuchel, Lydia; Roudier, Jean
CORPORATE SOURCE: INSERM EMI9940, Marseille, Fr.
SOURCE: Arthritis & Rheumatism (2002), 46(4), 929-933
CODEN: ARHEAW; ISSN: 0004-3591
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB HLA-DRB1 alleles whose third hypervariable region contains a QKRAA/QRRAA/RRRAA motif are assocd. with **rheumatoid arthritis** (**RA**) through unknown mechanisms. The

authors previously demonstrated that the QKRAA motif was also expressed on the Escherichia coli 40-kd heat-shock protein (HSP) **DnaJ**. The QKRAA motif helps **DnaJ** bind its partner chaperone, the E coli 70-kd HSP DnaK. Furthermore, the authors obsd. that in lymphoblastoid cells, Hsp73, the constitutive 70-kd HSP, assocs. with HLA-DRB1*0401 (an allele with a QKRAA motif) and targets it to lysosomes. In this study, the authors sought to classify different HLA-DRB1 alleles according to their ability to bind Hsp73. To evaluate how well different HLA-DRB1 alleles could bind Hsp73, the authors developed a quant. pptn. assay and a direct binding assay. Quant. pptn. assay from total cellular proteins and from lysosomal exts. demonstrated that RA-assocd. HLA-DRB1 alleles bound Hsp73 better than did HLA-DRB1 alleles that were not assocd. with RA. HLA-DRB1*0401 was the best Hsp73 binder. These findings were confirmed by direct binding assay between purified proteins. HLA-DRB1*0401 was the best Hsp73 binder among the 8 different HLA-DRB1 alleles that were tested.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:353472 HCAPLUS
DOCUMENT NUMBER: 136:368466
TITLE: Peptides derived from heat shock proteins for modulation of immune responses
INVENTOR(S): Martini, Alberto; Albani, Salvatore; Carson, Dennis A.; Prakken, Berent J.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002036611	A2	20020510	WO 2001-US45344	20011031
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002020038	A5	20020515	AU 2002-20038	20011031
US 2003031679	A1	20030213	US 2001-1938	20011031

PRIORITY APPLN. INFO.: US 2000-245181P P 20001101
WO 2001-US45344 W 20011031

AB The authors disclose a therapeutic strategy for ameliorating the inflammation-related symptoms of an immune-mediated disease, such as arthritis. The method comprises the administration of a bacterial **dnaJ** peptide, a human homolog peptide, or a non-homologous

human isoform. In one example, the authors demonstrate a proinflammatory response by oliogoarticular arthritis-derived synovial fluid T-cells to peptides derived from Escherichia coli **dnaJ**. This proinflammatory response was cross-reactive with peptides derived from homologous regions of HSJ1, HDJ1, or HDJ2. In contrast, stimulation of synovial T-cells with a non-homologous peptide derived from HSJ1 led to expansion of regulatory T-cells and prodn. of interleukin-10.

L8 ANSWER 14 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:185378 HCAPLUS
DOCUMENT NUMBER: 136:212896
TITLE: Gene markers useful for detecting skin damage in response to ultraviolet radiation
INVENTOR(S): Blumenberg, Miroslav
PATENT ASSIGNEE(S): New York University School of Medicine, USA
SOURCE: PCT Int. Appl., 274 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020849	A2	20020314	WO 2001-US28214	20010907
W: AU, CA, JP, SG				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
AU 2001090699	A5	20020322	AU 2001-90699	20010907

PRIORITY APPLN. INFO.: US 2000-231061P P 20000908
WO 2001-US28214 W 20010907

AB The cellular response to UV radiation exposure has been characterized on the mol. level through the use of high d. gene array technol. Nucleic acid mols. and protein mols., the expression of which are repressed or induced in response to UV radiation exposure, are identified according to a temporal pattern of altered expression post UV radiation exposure. Methods are disclosed that utilized these UV radiation-regulated mols. as markers for UV radiation exposure. Other screening methods of the invention are designed for the identification of compds. that modulate the response of a cell to UV radiation exposure. The invention also provides compns. useful for drug screening or pharmaceuticals purposes.

L8 ANSWER 15 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:185375 HCAPLUS
DOCUMENT NUMBER: 136:212895
TITLE: Screening methods to identify compounds that modulate a gene expression response of a cell to ultraviolet radiation exposure
INVENTOR(S): Blumenberg, Miroslav
PATENT ASSIGNEE(S): New York University, USA
SOURCE: PCT Int. Appl., 459 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020846	A2	20020314	WO 2001-US28040	20010907
W: AU, CA, JP, SG				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
US 2002090624	A1	20020711	US 2001-947870	20010906
AU 2001090658	A5	20020322	AU 2001-90658	20010907
PRIORITY APPLN. INFO.:			US 2000-231454P P	20000908
			WO 2001-US28040 W	20010907

AB The cellular response to UV radiation exposure has been characterized on the mol. level through the use of high d. gene array technol. Nucleic acid mols. and protein mols., the expression of which are repressed or induced in response to UV radiation exposure, are identified according to a temporal pattern of altered expression post UV radiation exposure. Gene and protein sequences regulated by exposure to UV-B or UV-A radiation in cultures of epidermal keratinocytes from human foreskin are provided. Methods are disclosed that utilized these UV radiation-regulated mols. as markers for UV radiation exposure. Other screening methods of the invention are designed for the identofication of compds. that modulate the response of a cell to UV radiation exposure. The invention also provides compns. useful for drug screening or pharmaceutical purposes.

L8 ANSWER 16 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:72748 HCAPLUS
DOCUMENT NUMBER: 136:146104
TITLE: Human stress genes identified using DNA microarrays
INVENTOR(S): Chenchik, Alex; Lukashev, Matvey E.
PATENT ASSIGNEE(S): Clontech, USA
SOURCE: U.S. Pat. Appl. Publ., 57 pp., Cont.-in-part of U.S. Ser. No. 441,920.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002009730	A1	20020124	US 2001-782909	20010213
PRIORITY APPLN. INFO.:			US 1998-222256 B2	19981228
			US 1999-440305 B2	19991117
			US 1999-441920 A2	19991117

AB Human stress arrays and methods for their use are provided. The subject arrays include a plurality of polynucleotide spots, each of which is made up of a polynucleotide probe compn. of unique polynucleotides corresponding to a human stress gene. The av. length of the polynucleotide probes is between 50 to 1000 nucleotides. The d. of the spots on the array did not exceed 400/cm2 and the spots had a diam. ranging between 10 to 5000 .mu.m. Furthermore, the no. of polynucleotide probe spots on the array ranged between 50 to 2000 nucleotides. The subject arrays find use in hybridization assays, particularly in assays for the

identification of differential gene expression of human stress genes. 236 Different human stress genes were identified using this approach.

L8 ANSWER 17 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:41632 HCAPLUS
DOCUMENT NUMBER: 136:117361
TITLE: Stress proteins as **immunomodulators** and in vaccines as fusion proteins with antigens
INVENTOR(S): Young, Richard A.
PATENT ASSIGNEE(S): Whitehead Institute for Biomedical Research, USA
SOURCE: U.S., 29 pp., Cont.-in-part of WO9429459.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6338952	B1	20020115	US 1994-336251	19941103
WO 8912455	A1	19891228	WO 1989-US2619	19890615
W: JP				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
WO 9429459	A1	19941222	WO 1994-US6362	19940606
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1221488	A1	20020710	EP 2001-203598	19940606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
US 6335183	B1	20020101	US 1995-461722	19950605
US 6482614	B1	20021119	US 1999-468041	19991221
US 2003073094	A1	20030417	US 2002-46649	20020114

PRIORITY APPLN. INFO.:

US 1988-207298	B2	19880615
US 1989-366581	B1	19890615
WO 1989-US2619	A2	19890615
US 1991-804632	B2	19911209
US 1993-73381	B2	19930604
WO 1994-US6362	A2	19940606
EP 1994-919384	A3	19940606
US 1994-336251	B1	19941103
US 1995-461720	B1	19950605

AB The present invention relates to stress proteins and methods of modulating an individual's immune response. In particular, it relates to the use of such stress proteins in immune therapy and prophylaxis, which results in an induction or enhancement of an individual's immune response and as an immunotherapeutic agent which results in a decrease of an individual's immune response to his or her own cells. The present invention also relates to compns. comprising a stress protein joined to another component, such as a fusion protein in which a stress protein is fused to an antigen. Further, the present invention relates to a method of generating antibodies to a substance using a conjugate comprised of a stress protein joined to the substance.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:473659 HCAPLUS
DOCUMENT NUMBER: 135:205729
TITLE: Microarray analysis of the in vivo effects of hypophysectomy and growth hormone treatment on gene expression in the rat
AUTHOR(S): Flores-Morales, Amilcar; Stahlberg, Nina; Tollet-Egnell, Petra; Lundeberg, Joakim; Malek, Renae L.; Quackenbush, John; Lee, Norman H.; Norstedt, Gunnar
CORPORATE SOURCE: Department of Molecular Medicine, Karolinska Institute, Stockholm, 17176, Swed.
SOURCE: Endocrinology (2001), 142(7), 3163-3176
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors used cDNA microarrays contg. 3000 different rat genes to study the consequences of severe hormonal deficiency (hypophysectomy) on the gene expression patterns in heart, liver, and kidney. Hybridization signals were seen from a majority of the arrayed cDNAs; nonetheless, tissue-specific expression patterns could be delineated. Hypophysectomy affected the expression of genes involved in a variety of cellular functions. Between 16-29% of the detected transcripts from each tissue changed expression level as a reaction to this condition. Chronic treatment of hypophysectomized animals with human GH also caused significant changes in gene expression patterns. The study confirms previous knowledge concerning certain gene expression changes in the above-mentioned situations and provides new information regarding hypophysectomy and chronic human GH effects in the rat. Furthermore, the authors have identified several new genes that respond to GH treatment. The results represent a first step toward a more global understanding of gene expression changes in states of hormonal deficiency.
REFERENCE COUNT: 92 THERE ARE 92 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 19 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:320130 HCAPLUS
DOCUMENT NUMBER: 134:348982
TITLE: Synthetic human genes and chimeric autoantigens and their use in diagnosis and treatment of autoimmune diseases
INVENTOR(S): Ben-Nun, Avraham; Kerlero De Rosbo, Nicole; Sappler, Gregor Paul
PATENT ASSIGNEE(S): Yeda Research and Development Co. Ltd., Israel
SOURCE: PCT Int. Appl., 182 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001031037 A2 20010503 WO 2000-IL688 20001026
WO 2001031037 A3 20020711
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1238089 A2 20020911 EP 2000-971684 20001026
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL
PRIORITY APPLN. INFO.: IL 1999-132611 A 19991027
WO 2000-IL688 W 20001026

AB Synthetic human target autoantigen genes comprising sequences coding for at least two immunogenic epitopic clusters (hereinafter IEC) of autoantigen(s) related to a specific autoimmune disease, wherein said at least two IECs may be derived from a single autoantigen or from .gtoreq.2 different autoantigens related to said autoimmune disease, and proteins encoded thereby, can be used for the treatment and the diagnosis of autoimmune diseases such as multiple sclerosis (MS), insulin-dependent diabetes mellitus (IDDM), **rheumatoid arthritis** (**RA**), myasthenia gravis (MG) and uveitis. Thus, synthetic human multi-target autoantigen genes (shMultiTAG) were prepd. and expressed in Escherichia coli. One such shMultiTAG encoded a fusion protein comprising 3 epitopes of each of 4 proteins, i.e., myelin oligodendrocyte glycoprotein, myelin basic protein, proteolipid protein, and myelin-oligodendrocytic basic protein. This recombinant protein, or the DNA encoding it, modulated exptl. autoimmune encephalitis in mice.

L8 ANSWER 20 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:312014 HCAPLUS
DOCUMENT NUMBER: 136:64938
TITLE: Toward elucidating the global gene expression patterns of developing Arabidopsis: parallel analysis of 8 300 genes by a high-density oligonucleotide probe array
AUTHOR(S): Zhu, Tong; Budworth, Paul; Han, Bin; Brown, Devon; Chang, Hur-Song; Zou, Guangzhou; Wang, Xun
CORPORATE SOURCE: Torrey Mesa Research Institute, Inc., San Diego, CA, 92121, USA
SOURCE: Plant Physiology and Biochemistry (Paris, France) (2001), 39(3-4), 221-242
CODEN: PPBIEX; ISSN: 0981-9428
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Arabidopsis thaliana has been widely used as a model system, in various aspects of biol. studies, such as genomics, genetics, cellular, developmental and mol. biol. In order to reveal the mol. events and regulatory networks controlling Arabidopsis development and responses to genetic and environmental changes, we designed and used a high-d. oligonucleotide probe array (GeneChip) to profile

global gene expression patterns. The Arabidopsis oligonucleotide probe array consists of probes from 8 300 unique Arabidopsis genes, which covers approx. one-third of the genome. Global transcription profiles of A. thaliana in various developmental stages, and their responses to different environments were generated using this microarray, and archived. Here, we analyze data sets derived from nineteen independent expts. Constitutively and differentially expressed genes in seedlings, roots, leaves, inflorescences, flowers and siliques at different developmental stages were identified. Functions of these genes based on homologs were detd. and categorized. Our results provide insight into the coordinated transcriptional regulation of the genes during plant growth and development.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 21 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:287556 HCAPLUS
DOCUMENT NUMBER: 135:330374
TITLE: Immunodominant region of Actinobacillus actinomycetemcomitans 40-kilodalton heat shock protein in patients with **rheumatoid arthritis**
AUTHOR(S): Yoshida, A.; Nakano, Y.; Yamashita, Y.; Oho, T.; Ito, H.; Kondo, M.; Ohishi, M.; Koga, T.
CORPORATE SOURCE: Department of Oral and Maxillofacial Oncology and Department of Preventive Dentistry, Faculty of Dental Science, Kyushu University, Fukuoka, 812-8582, Japan
SOURCE: Journal of Dental Research (2001), 80(1), 346-350
CODEN: JDREAF; ISSN: 0022-0345
PUBLISHER: International Association for Dental Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bacterial heat shock proteins have been implicated in the pathogenesis of several diseases, and the immunol. relationship between **rheumatoid arthritis** (**RA**) and Escherichia coli **DnaJ** has been reported. Since there are similarities in the tissue destruction process of RA and periodontitis, we examd. the reactivities of antibodies in sera from RA patients to the **DnaJ** protein from Actinobacillus actinomycetemcomitans. An ELISA showed that IgG titers to the N-terminal conservative region of the **DnaJ** are significantly higher in RA patients compared with the healthy controls ($p < 0.05$). Furthermore, we examd. IgG titers of disease controls to det. the specificity of the immune responses to this region in RA patients. The difference between RA and infectious disease patients was also significant ($p < 0.05$). These results suggest that the N-terminal region of **DnaJ** from A. actinomycetemcomitans may contribute to the etiol. anal. of RA.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 22 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:243120 HCAPLUS

DOCUMENT NUMBER: 133:236729
TITLE: **Immunomodulatory** effects by a heat shock protein **dnaJ**-derived peptide in **rheumatoid arthritis**
AUTHOR(S): Samodal, Rodrigo T.; Albani, Salvatore
CORPORATE SOURCE: Departments of Medicine and Pediatrics, University of California, San Diego, La Jolla, CA, 92093-0663, USA
SOURCE: Verhandelingen - Koninklijke Nederlandse Akademie van Wetenschappen, Afdeling Natuurkunde, Tweede Reeks (1999), 101(Specific Immunotherapy of Chronic Autoimmune Diseases), 63-71
CODEN: VNAWAG; ISSN: 0373-465X
PUBLISHER: Royal Netherlands Academy of Arts and Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Peptides derived from the E. coli heat shock protein (hsp) **dnaJ** share the "shared epitope" sequence with HLA DR alleles assocd. with **rheumatoid arthritis**. These peptides are antigenic in human autoimmune arthritis. T cell recognition of these peptides is assocd. with TH-1 type and pro-inflammatory responses, including prodn. of TNF.alpha., suggesting an involvement of these abnormal responses in the pathogenesis of autoimmune inflammation. In a pilot clin. trial, we attempted to modulate these pro-inflammatory responses by oral administration of various doses (.25, 2.5, 25 mg po qd for 6 mo) of the target antigen in 15 patients with **rheumatoid arthritis**. We measured the percentage of CD3+ cells producing the pro-inflammatory cytokines IL2, IFN.gamma., TNF.alpha., and the tolerogenic cytokines IL4 and IL10, by FACS anal. of the intracellular products. In addn., we measured the cytokine concns., including **TGF.beta.**, by ELISA in culture supernatant. The obsd. decline in pro-inflammatory cytokines prodn. during treatment was accompanied by IL4, IL10 and **TGF.beta.** prodn., suggesting an effective **immunomodulation** of these disease-specific responses.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 23 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:453566 HCAPLUS
DOCUMENT NUMBER: 132:11483
TITLE: Isolation of an IgG monoclonal anti-**dnaJ** antibody from an immunoglobulin combinatorial library from a patient with **rheumatoid arthritis**
AUTHOR(S): Chukwuocha, Reginald U.; Zhang, Baoping; Lai, Chung-Jeng; Scavulli, John F.; Albani, Salvatore; Carson, Dennis A.; Chen, Pojen P.
CORPORATE SOURCE: Department of Medicine/Rheumatology, University of California, Los Angeles, CA, 90095-1670, USA
SOURCE: Journal of Rheumatology (1999), 26(7), 1439-1445
CODEN: JRHUA9; ISSN: 0315-162X
PUBLISHER: Journal of Rheumatology Publishing Co. Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previously, we showed that **rheumatoid arthritis** (**RA**) had both antibodies and T cells specific for the QKRAA-encompassing Escherichia coli **dnaJ** protein. These findings suggest that the bacteria induced anti-**dnaJ** responses may cross react with the human homolog of bacterial **dnaJ** in the joint, resulting in tissue damage. We used the combinatorial library technique to isolate and characterize an IgG monoclonal anti-**dnaJ** antibody (designated CG1) from the blood of a patient with RA. Sequence anal. of CG1 revealed that its heavy and light chain V regions were resp. most homologous to the 3d279d VH4 and the O18 Vk1 genes. Interestingly, 3d279d is frequently expressed by B cells stimulated with staphylococcal enterotoxin; and O18 is the main gene employed by the Vk1 IgG antibodies against Haemophilus influenzae. The combinatorial Ig library method represents an interesting model of how to approach the isolation and characterization of antibody-like reagents in the elucidation of autoantigens in RA.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 24 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:132810 HCAPLUS
DOCUMENT NUMBER: 130:336833
TITLE: Overexpression of human homologs of the bacterial **DnaJ** chaperone in the synovial tissue of patients with **rheumatoid arthritis**
AUTHOR(S): Kurzik-Dumke, Ursula; Schick, Christoph; Rzepka, Rita; Melchers, Inga
CORPORATE SOURCE: Johannes Gutenberg University, Mainz, Germany
SOURCE: Arthritis & Rheumatism (1999), 42(2), 210-220
CODEN: ARHEAW; ISSN: 0004-3591
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The objective of this study was to study the expression of the chaperone family of J proteins in the synovial tissue of patients with **rheumatoid arthritis** (**RA**) or osteoarthritis. Rabbit antibodies specific for a synthetic peptide (pHSJ1: EAYEVLSDKHKREIYD), representing the most conserved part of all J domains thus far identified-among them the Drosophila tumor suppressor Tid56-were used in immunohistochem. analyses of frozen sections of synovial tissue and immunoblotting of protein exts. of adherent synovial cells. IgG specific for Tid56 was also used. Both antisera predominantly and intensely stained synovial lining cells from RA patients; other cells did not stain or stained only faintly. In immunoblots, anti-pHSJ1 specifically detected several bands with mol. wts. of >74 kDa (type I), 57-64 kDa (type II), 41-48 kDa (type III), and .ltoreq.36 kDa (type IV). The strongest band detected in RA adherent synovial cells was the type II band, whereas in a B cell line, a type I band was prominent. Several potentially new members of the J family are described. The type II band represents the human homolog of the Drosophila Tid56 protein and is strongly expressed in RA synovial tissue.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 25 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:806683 HCAPLUS
DOCUMENT NUMBER: 130:62038
TITLE: Cloning and cDNA sequences of two new human **DnaJ**-like proteins
INVENTOR(S): Au-Young, Janice; Lal, Preeti; Bandman, Olga
PATENT ASSIGNEE(S): Incyte Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9855509	A2	19981210	WO 1998-US11182	19980602
WO 9855509	A3	19990325		
W: AT, AU, BR, CA, CH, CN, DE, DK, ES, FI, GB, IL, JP, KR, MX, NO, NZ, RU, SE, SG, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5922567	A	19990713	US 1997-868288	19970603
AU 9877143	A1	19981221	AU 1998-77143	19980602
US 6001598	A	19991214	US 1999-235373	19990120
US 6043222	A	20000328	US 1999-388993	19990902

PRIORITY APPLN. INFO.: US 1997-868288 19970603
WO 1998-US11182 19980602
US 1999-235373 19990120

AB The invention provides a two new human **DnaJ**-like proteins (HSPJ1 or HSPJ2) and polynucleotides which identify and encode HSPJ1 or HSPJ2. Nucleic acids encoding HSPJ1 and HSPJ2 were first identified in Incyte clones 136466 and 260873 from a synovial membrane tissue or hNT2 cDNA library, resp., through a computer search for amino acid sequence alignments; consensus sequences were derived from overlapping and/or extended nucleic acid sequences. The proteins are 358 and 330 amino acids in length and possess potential **DnaJ** domains and chem. and structural homol. with **DnaJ**-2, HSJ1a, and HSJ1b. Northern anal. shows the expression of these sequences in various libraries, at least 46% of which are immortalized or cancerous. The invention also provides expression vectors, host cells, agonists, antibodies and antagonists. The invention also provides methods for treating disorders assocd. with expression of HSPJ1 or HSPJ2.

L8 ANSWER 26 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:765634 HCAPLUS
DOCUMENT NUMBER: 130:137555
TITLE: Cellular gene expression altered by human cytomegalovirus: global monitoring with oligonucleotide arrays
AUTHOR(S): Zhu, Hua; Cong, Jian-Ping; Mamtora, Gargi; Gingeras, Thomas; Shenk, Thomas
CORPORATE SOURCE: Howard Hughes Medical Institute, Department of Molecular Biology, Princeton University, Princeton, NJ, 08544, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1998), 95(24), 14470-14475
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mechanistic insights to viral replication and pathogenesis generally have come from the anal. of viral gene products, either by studying their biochem. activities and interactions individually or by creating mutant viruses and analyzing their phenotype. Now it is possible to identify and catalog the host cell genes whose mRNA levels change in response to a pathogen. We have used DNA array technol. to monitor the level of .apprxeq.6,600 human mRNAs in uninfected as compared with human cytomegalovirus-infected cells. The level of 258 mRNAs changed by a factor of 4 or more before the onset of viral DNA replication. Several of these mRNAs encode gene products that might play key roles in virus-induced pathogenesis, identifying them as intriguing targets for further study.

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 27 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:618833 HCAPLUS
DOCUMENT NUMBER: 129:225726
TITLE: Pharmaceutical or food composition for treating pathologies related to graft-versus-host disease or allergic or autoimmune reactions
INVENTOR(S): Duchateau, Jean; Servais, Genevieve
PATENT ASSIGNEE(S): Universite Libre De Bruxelles, Belg.
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9839029	A2	19980911	WO 1998-BE30	19980305
WO 9839029	A3	19990114		
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
BE 1011033	A6	19990406	BE 1997-199	19970305
EP 975362	A2	20000202	EP 1998-909232	19980305
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE				
JP 2001514623	T2	20010911	JP 1998-538003	19980305
US 6312711	B1	20011106	US 1999-380548	19991028

PRIORITY APPLN. INFO.: BE 1997-199 A 19970305
WO 1998-BE30 W 19980305

AB The invention concerns a pharmaceutical and/or food compn. comprising a suitable pharmaceutical and/or food vehicle and a heat shock protein and at least conformation or sequential epitopes of an antigenic structure inducing a graft vs. host, an allergic or autoimmune reaction.

L8 ANSWER 28 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:441966 HCAPLUS
DOCUMENT NUMBER: 129:94461
TITLE: Vaccine compositions and methods useful in inducing immune protection against **arthritogenic** peptides involved in the pathogenesis of **rheumatoid arthritis**
INVENTOR(S): Carson, Dennis A.; Albani, Salvatore
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: U.S., 18 pp., Cont.-in-part of U. S. Ser. No. 246,988, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5773570	A	19980630	US 1996-618464	19960315
HU 76359	A2	19970828	HU 1996-3214	19950424
HU 220101	B	20011028		
CA 2247804	AA	19970918	CA 1997-2247804	19970220
WO 9734002	A1	19970918	WO 1997-US2957	19970220
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9719755	A1	19971001	AU 1997-19755	19970220
AU 727087	B2	20001130		
EP 923646	A1	19990623	EP 1997-907862	19970220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 331989	A	20000128	NZ 1997-331989	19970220
JP 2000507232	T2	20000613	JP 1997-532622	19970220
US 6153200	A	20001128	US 1998-107615	19980630
NO 9804244	A	19981116	NO 1998-4244	19980914

PRIORITY APPLN. INFO.: US 1994-246988 B2 19940520
US 1996-618464 A 19960315
WO 1997-US2957 W 19970220

AB Vaccine compns. useful in inducing immune protection in a host against **arthritogenic** peptides involved in the pathogenesis of **rheumatoid arthritis** are disclosed. Each vaccine compn. provides antigenic **dnaJp1** peptide (by including the peptide or a polynucleotide which encodes the peptide).

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 29 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:625612 HCAPLUS
DOCUMENT NUMBER: 127:277197

TITLE: Antigens for use in inducing immune tolerance to **arthritogenic** peptides and protection against **rheumatoid arthritis**
INVENTOR(S): Carson, Dennis A.; Albani, Salvatore
PATENT ASSIGNEE(S): Regents of the University of California, USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9734002	A1	19970918	WO 1997-US2957	19970220
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5773570	A	19980630	US 1996-618464	19960315
AU 9719755	A1	19971001	AU 1997-19755	19970220
AU 727087	B2	20001130		
EP 923646	A1	19990623	EP 1997-907862	19970220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 331989	A	20000128	NZ 1997-331989	19970220
JP 2000507232	T2	20000613	JP 1997-532622	19970220
NO 9804244	A	19981116	NO 1998-4244	19980914

PRIORITY APPLN. INFO.:
US 1996-618464 A 19960315
US 1994-246988 B2 19940520
WO 1997-US2957 W 19970220

AB Peptides that can be used in compns. that induce immune tolerance to peptides contg. the sequence Q(K/R)RAA that is found in some HLA proteins are described. This induces tolerance to a range of **arthritogenic** peptides involved in the pathogenesis of **rheumatoid arthritis**. Specifically, the **arthritogenic** peptides are derived from the **DnaJ** protein or its homologs. A vaccine including these peptides, or a vector vaccine encoding them may be used. Alternatively, IgA antibodies to the peptides can be used, preferably as Fab fragments, to induce tolerance. Methods of identifying individuals susceptible to, or at risk for, developing **rheumatoid arthritis** are also described. **DnaJ** of Escherichia coli was found to induce cellular proliferation in peripheral blood lymphocytes of early stage **rheumatoid arthritis**.

L8 ANSWER 30 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:259936 HCAPLUS
DOCUMENT NUMBER: 126:329398
TITLE: A function for the QKRAA amino acid motif: mediating binding of **DNaJ** to DnaK. Implications for the Association of **Rheumatoid Arthritis** with HLA-DR4

AUTHOR(S): Auger, Isabelle; Roudier, Jean
CORPORATE SOURCE: Laboratoire d'Immuno Rhumatologie, Faculte Medecine Marseille, Marseille, 13005, Fr.
SOURCE: Journal of Clinical Investigation (1997), 99(8), 1818-1822
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The amino acid motif QKRAA, when expressed on HLA-DRB1, carries susceptibility to develop **rheumatoid arthritis**. This motif is the basis of strong B and T cell epitopes. Furthermore, it is highly overrepresented in protein data-bases, suggesting that it carries a function of its own. To identify this function, we used QKRAA peptide affinity columns to screen total protein exts. from Escherichia coli. We found that DnaK, the E. coli 70-kD heat shock protein, binds QKRAA. Of interest, DnaK has a natural ligand, **DnaJ**, that contains a QKRAA motif. We found that QKRAA-contg. peptides inhibit the binding of DnaK to **DnaJ**. Furthermore, rabbit antibody to the QKRAA motif can inhibit binding of **DnaJ** to DnaK. These data suggest that QKRAA mediates the binding of E. coli chaperone **DnaJ** to its partner chaperone DnaK.

L8 ANSWER 31 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:625975 HCAPLUS
DOCUMENT NUMBER: 125:272836
TITLE: A multistep molecular mimicry hypothesis for the pathogenesis of **rheumatoid arthritis**
AUTHOR(S): Albani, Salvatore; Carson, Dennis A.
CORPORATE SOURCE: Dep. Pediatrics, Univ. California, San Diego, La Jolla, CA, 92093-0663, USA
SOURCE: Immunology Today (1996), 17(10), 466-470
CODEN: IMTOD8; ISSN: 0167-4919
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 52 refs. Pos. selected T cells might be involved in physiol. immune responses to exogenous antigens as well as in abnormal processes leading to autoimmune disease. Here, the authors discuss this notion in the context of a multistep mol. mimicry hypothesis for the etiopathogenesis of **rheumatoid arthritis**, based on the shared epitope, a peptide sequence that is shared by virtually all the HLA alleles correlated to the disease.

L8 ANSWER 32 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:113371 HCAPLUS
DOCUMENT NUMBER: 124:173427
TITLE: **Arthritogenic** intestinal flora replacement and method and vaccines for the treatment of **rheumatoid arthritis**
INVENTOR(S): Carson, Dennis A.; Salvatore, Albani
PATENT ASSIGNEE(S): Reagents of the University of California, USA
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9531984	A1	19951130	WO 1995-US4896	19950424
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9523600	A1	19951218	AU 1995-23600	19950424
AU 696646	B2	19980917		
EP 762881	A1	19970319	EP 1995-917611	19950424
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
HU 76359	A2	19970828	HU 1996-3214	19950424
HU 220101	B	20011028		
JP 10500679	T2	19980120	JP 1995-530288	19950424
NZ 284914	A	20000825	NZ 1995-284914	19950424
FI 9604604	A	19970115	FI 1996-4604	19961118
NO 9604910	A	19961119	NO 1996-4910	19961119

PRIORITY APPLN. INFO.: US 1994-246988 A 19940520
WO 1995-US4896 W 19950424

AB Methods useful in the treatment or prevention of **rheumatoid arthritis** (**RA**) are disclosed. Each method is useful in limiting the exposure of the systemic immune system of a human to **RA arthritogenic** peptides present in the person's gastrointestinal (GI) tract. To this end, one method of the invention reduces the population of **arthritogenic** peptide-producing bacteria in the GI tract (e.g., by means of antibiotics) then replaces those bacteria with ones incapable of producing the **arthritogenic** peptides (e.g., bacteria altered by site-directed mutagenesis to express heat-shock protein **dnaJ** contg. the motif DERAAYDQYGHAAFE instead of QKRAAYDQYGHAAFE). Methods for both passive and active immunization of a human against **arthritogenic** peptides are disclosed, as in a method for identifying persons who are predisposed to develop **RA**.

L8 ANSWER 33 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:560363 HCAPLUS
DOCUMENT NUMBER: 122:312551
TITLE: Positive selection in autoimmunity: Abnormal immune responses to a bacterial **dnaJ** antigenic determinant in patients with early **rheumatoid arthritis**
AUTHOR(S): Albani, Salvatore; Keystone, Edward C.; Nelson, J. Lee; Ollier, William E. R.; La Cava, Antonio; Montemayor, Ann C.; Weber, Deborah A.; Montecucco, Carlomaurizio; Martini, Alberto; et al.
CORPORATE SOURCE: Sand and Rose Stein Institute Research on Aging, University California, La Jolla, CA, 92093-0663,

USA
SOURCE: Nature Medicine (New York) (1995), 1(5), 448-52
CODEN: NAMEFI; ISSN: 1078-8956
PUBLISHER: Nature Publishing Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A novel multistep mimicry mechanism for induction of **rheumatoid arthritis** (**RA**) by bacterial antigens that activate T lymphocytes previously educated by peptides derived from a class of human histocompatibility antigens is reported here. These antigens have the amino acid sequence QKRAA, which is also present on the Escherichia coli heat-shock protein **dnaJ**. Synovial fluid cells of early RA patients have strong immune responses to the bacterial antigen, but cells from normal subjects or controls with other autoimmune diseases do not. The activated T cells may cross-react with autologous **dnaJ** heat-shock proteins that are expressed at synovial sites of inflammation. Our findings may have direct relevance to new strategies for the immune therapy of RA.

L8 ANSWER 34 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:557073 HCAPLUS
DOCUMENT NUMBER: 119:157073
TITLE: Heat shock (stress) proteins and autoimmunity in rheumatic diseases
AUTHOR(S): Schultz, Duane R.; Arnold, Patricia I.
CORPORATE SOURCE: Sch. Med., Univ. Miami, Miami, FL, USA
SOURCE: Seminars in Arthritis and Rheumatism (1993), 22(6), 357-74
CODEN: SAHRBF; ISSN: 0049-0172
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 132 refs. Topics discussed include: characteristics of heat shock (stress) proteins, role of microbial heat shock proteins and mol. mimicry in rheumatic diseases, T-lymphocytes and heat shock proteins, humoral immunity and heat shock proteins, other studies of autoimmunity and heat shock proteins, the dnaK, **dnaJ**, and grpE heat shock proteins of Escherichia coli, autoimmunity, heat shock proteins, and systemic lupus erythematosus, and .gamma..delta. T cells in **rheumatoid arthritis** .

L8 ANSWER 35 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:549144 HCAPLUS
DOCUMENT NUMBER: 117:149144
TITLE: Molecular basis for the association between HLA DR4 and **rheumatoid arthritis** . From the shared epitope hypothesis to a peptidic model of **rheumatoid arthritis**
AUTHOR(S): Albani, Salvatore; Roudier, Jean
CORPORATE SOURCE: Inst. Aging, Univ. California, San Diego, La Jolla, CA, 92037, USA
SOURCE: Clinical Biochemistry (1992), 25(3), 209-12
CODEN: CLBIAS; ISSN: 0009-9120
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Susceptibility to **rheumatoid arthritis** (

RA) maps to residues QKRAA/QRRAA in the 3rd hypervariable region of the HLA DR.beta.1 chain. Peptides from the same area of MHC class II mols. are able to modulate the T-cell repertoire by deleting self-reactive T-cells. The Epstein Barr virus glycoprotein gp110 and the **DNA J** heat-shock protein from Escherichia coli mimic the 3rd hypervariable region of HLA-Dw4DR.beta.1. Thus, the same area of HLA DR.beta.1 carries susceptibility to RA, modulates the T-cell repertoire, and is mimicked by human pathogens. RA may originate from a particular shape imposed on the T-cell repertoire by the QKRAA/QRRAA sequence in the 3rd hypervariable region of HLA DR.beta.1.

L8 ANSWER 36 OF 36 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:57226 HCAPLUS
DOCUMENT NUMBER: 116:57226
TITLE: The susceptibility sequence to **rheumatoid arthritis** is a cross-reactive B cell epitope shared by the Escherichia coli heat shock protein **dnaJ** and the histocompatibility leukocyte antigen DRB10401 molecule
AUTHOR(S): Albani, Salvatore; Tuckwell, Julia E.; Esparza, Lucia; Carson, Dennis A.; Roudier, Jean
CORPORATE SOURCE: Sam and Rose Stein Inst. Res. Aging, Univ. California, San Diego, La Jolla, CA, 92093-0945, USA
SOURCE: Journal of Clinical Investigation (1992), 89(1), 327-31
CODEN: JCINAO; ISSN: 0021-9738
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Immunol. responses to bacterial heat shock proteins have been implicated in the pathogenesis of arthritis in animals and humans. The predicted amino acid sequence of **dnaJ**, a heat shock protein from E. coli, contains an 11-amino acid segment that is homologous to the third hypervariable region of the human histocompatibility antigen (HLA) DRB10401 (formerly known as HLA Dw4), the part of the mol. that carries susceptibility to **rheumatoid arthritis**. To test the biol. significance of this finding, the authors expressed and purified recombinant **dnaJ** (rdnaJ), and detd. its immunol. cross-reactivity with HLA DRB10401. A rabbit antipeptide antiserum raised against the sequence of the third hypervariable region of HLA DRB10410 specifically bound to rdnaJ, thus confirming that a similar sequence is expressed on the bacterial protein. Of greater consequence, an antiserum to the rdnaJ protein recognized not only a peptide from the third hypervariable region of HLA DRB10401, but also the intact HLA DRB10401 polypeptide. Furthermore, the antibody to rdnaJ reacted with HLA DRB10401 homozygous B lymphoblasts, but not with HLA DRB11501, DRB10101, DRB10301, and DRB10701 (formerly known as HLA Dw2, DR 1, DR 3, and DR 7, in the same order) homozygous cells. Thus, exposure to a bacterial heat shock protein can elicit antibodies against the **rheumatoid arthritis** susceptibility sequence in the third hypervariable region of HLA DRB10401.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 10:33:39 ON 10 JUL 2003)

L9 7 SEA ABB=ON PLU=ON L6
L10 86 SEA ABB=ON PLU=ON L7
L11 57 SEA ABB=ON PLU=ON L10 AND (ESCHERICH? OR LACTOCOCC? OR KLEBSIELL? OR PROTEUS OR SALMONELLA)
L12 63 SEA ABB=ON PLU=ON L9 OR L11
L13 34 DUP REM L12 (29 DUPLICATES REMOVED)

L13 ANSWER 1 OF 34 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2003-393457 [37] WPIDS
DOC. NO. CPI: C2003-104565
TITLE: Identifying regions of neoplastic growth in a human body, useful for detecting or predicting metastasis, comprises administering to the human body an antibody or peptide that specifically binds to a protein marker of neoplastic growth.
DERWENT CLASS: B04 D16
INVENTOR(S): BARDELLI, A; KINZLER, K W; SAHA, S; VOGELSTEIN, B
PATENT ASSIGNEE(S): (UYJO) UNIV JOHNS HOPKINS
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003031930	A2	20030417	(200337)*	EN	42

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003031930	A2	WO 2002-US31247	20021002

PRIORITY APPLN. INFO: US 2001-327332P 20011009
AN 2003-393457 [37] WPIDS
AB WO2003031930 A UPAB: 20030612
NOVELTY - Identifying regions of neoplastic growth in a human body comprising administering to the human body an antibody or a peptide, which specifically binds to a protein marker of neoplastic growth, and detecting regions of the human body to which the antibody or peptide has specifically bound, is new.

DETAILED DESCRIPTION - Identifying regions of neoplastic growth in a human body comprising administering to the human body an antibody or a peptide, which specifically binds to a protein marker of neoplastic growth, and detecting regions of the human body to which the antibody or peptide has specifically bound, is new. The protein marker of neoplastic growth comprises protein tyrosine phosphatase type IVA member 3, FLJ23603, LOC54675, ZD52F10, **DNAJ** domain-containing, GRO3 oncogene/T45117 hU1-70K protein, attractin, Bcl-2 binding component 3, nuclear receptor subfamily 4, mitogen activated protein kinase 8 interacting protein 2, hairy (Drosophila)-homolog, LUC7 (Saccharomyces cerevisiae)-like,

transducin-like enhancer of split 2, homolog of Drosophila E (sp1), adipose differentiation-related protein, keratin 17, casein kinase 2, alpha prime polypeptide, minichromosome maintenance deficient (S. cerevisiae) 7, v-jun avian sarcoma virus 17 oncogene homolog/LSFR2 gene 2/MGC2550 protein, plexin B1, **transforming growth factor, beta** 1ESTs, similar to GTP-rho binding protein 1 (rhophilin), (Drosophila)-like homeo box imago-nashi (Drosophila) homolog, proliferation-associated, putative Rab5-interacting protein vascular endothelial growth factor, PTD008 protein, protein/ribosomal protein L10, weel pos. (Schizosaccharomyces pombe) homolog/protein multiply 013, cDNA:FLJ12683, PTK7 protein tyrosine kinase 7v-fos FBJ murine osteosarcoma viral oncogene homolog B, FLJ20297 protein SET translocation (myeloid leukemia-associated), chaperonin containing TCP1, subunit 6A (zeta 1), ataxin 2 related protein, cyclin-dependent kinase inhibitor 3 (CDK2-associated dual specificity phosphatase), or matrix metalloproteinase 14 (membrane-inserted). INDEPENDENT CLAIMS are included for the following:

(1) detecting or predicting metastasis;

(2) treating a patient with an advanced or metastatic cancer; and

(3) identifying candidate drugs for treating advanced or metastatic tumors.

ACTIVITY - Cytostatic.

No biological data given.

MECHANISM OF ACTION - Protein Tyrosine Phosphatase Inhibitor.

USE - The methods are useful for identifying regions of neoplastic growth in a human body. The methods are also useful for detecting or predicting metastasis, or identifying candidate drugs for treating advanced or metastatic tumors, e.g. gastrointestinal, prostate, breast or colorectal tumor or cancer. The antibodies or peptides that bind to the identified targets are useful for diagnostic imaging.

Dwg.0/4

L13 ANSWER 2 OF 34 MEDLINE DUPLICATE 1

ACCESSION NUMBER: 2003293084 IN-PROCESS
DOCUMENT NUMBER: 22704599 PubMed ID: 12820650
TITLE: Characterization of the anti-**DnaJ** monoclonal antibodies and their use to compare immunological properties of **DnaJ** and its human homologue HDJ-1.
AUTHOR: Krzewski Konrad; Kunikowska Danuta; Wysocki Jan; Kotlarz Agnieszka; Thompkins Philip; Ashraf William; Lindsey Nigel; Picksley Steven; Glosnicka Renata; Lipinska Barbara
CORPORATE SOURCE: Department of Biochemistry, University of Gdansk, Poland.
SOURCE: CELL STRESS AND CHAPERONES, (2003 Spring) 8 (1) 8-17. Journal code: 9610925. ISSN: 1355-8145.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20030625
Last Updated on STN: 20030625

AB **Escherichia** coli **DnaJ** (Hsp40) is suspected to

participate in **rheumatoid arthritis** (**RA**) pathogenesis in humans by an autoimmune process. In this work a set of 6 anti-**DnaJ** monoclonal antibodies (mAbs) was raised and localization of the epitopes recognized by the mAbs was investigated. Western blotting and enzyme-linked immunosorbent assay (ELISA) experiments showed that the mAbs efficiently bound only native antigen. Using **DnaJ** mutant proteins with deletions of specified domains and ELISA, we found that AC11 mAb reacted with the best conserved in evolution N-terminal J domain, whereas BB3, EE11, CC5, CC8, and DC7 bound to the C-terminal part after residue 200. Mapping performed with the use of a random peptide library displayed by filamentous phage indicated that (1) AC11 mAb bound to a region between residues 33-48, including D-34 which belongs to the HPD triad, present in all **DnaJ** homologues, (2) BB3 recognized residues localized in the 204-224 region, (3) EE11 recognized the 291-309 region, (4) CC5--the region 326-359, and (5) CC8--the 346-366 region. All these mAbs, as well as the polyclonal antibodies against the N- or C-terminal domain, bound efficiently to HDJ-1, human Hsp40. These results show the presence of a significant immunological similarity between bacterial **DnaJ** and human HDJ-1, which is not restricted to the evolutionarily conserved parts of the proteins, and suggest that HDJ-1 could be a possible target of immune response triggered by **DnaJ**.

L13 ANSWER 3 OF 34 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-489999 [52] WPIDS
DOC. NO. CPI: C2002-139110
TITLE: New **immunomodulatory** peptides from heat shock proteins, useful for treating immunological disorder in subjects such as humans, e.g. autoimmune disease (e.g. arthritis), infectious disease, inflammatory bowel disease or cancer.
DERWENT CLASS: B04 D16
INVENTOR(S): ALBANI, S; CARSON, D A; MARTINI, A; PRAKKEN, B J
PATENT ASSIGNEE(S): (MART-I) MARTINI A; (REGC) UNIV CALIFORNIA; (ALBA-I) ALBANI S; (CARS-I) CARSON D A; (PRAK-I) PRAKKEN B J
COUNTRY COUNT: 98
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002036611	A2	20020510	(200252)*	EN	84
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2002020038	A	20020515	(200258)		
US 2003031679	A1	20030213	(200314)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

WO 2002036611 A2	WO 2001-US45344	20011031
AU 2002020038 A	AU 2002-20038	20011031
US 2003031679 A1 Provisional	US 2000-245181P	20001101
	US 2001-1938	20011031

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002020038 A	Based on	WO 200236611

PRIORITY APPLN. INFO: US 2000-245181P 20001101; US 2001-1938 20011031

AN 2002-489999 [52] WPIDS

AB WO 200236611 A UPAB: 20020815

NOVELTY - A peptide, which is an immunogenic portion derived from a **dnaJ** heat shock protein (hsp), comprising any of 26 amino acid sequences fully defined in the specification, is new.

DETAILED DESCRIPTION - A peptide comprising any of sequences P1-P26, which is an immunogenic portion derived from a **dnaJ** hsp, is new.

(1) P1: Gln-Asp-Tyr-Tyr-Glu-Ile-Leu-Gly-Val-Ser-Lys-Thr-Ala-Glu-Glu;

(2) P2: Arg-Lys-Ala-Tyr-Lys-Arg-Leu-Ala-Met-Lys-Tyr-His-Pro-Asp-Arg;

(3) P3: Gln-Lys-Arg-Ala-Ala-Tyr-Asp-Gln-Tyr-Gly-His-Ala-Ala-Phe-Glu-Gln;

(4) P4: Gln-Gly-Phe-Phe-Ala-Val-Gln-Gln-Thr-Cys-Pro-His-Cys-Gln-Gly;

(5) P5: Ser-Lys-Thr-Leu-Ser-Val-Lys-Ile-Pro-Gly-Ala-Val-Asp-Thr-Gly;

(6) P6: Gly-Asp-Leu-Tyr-Val-Gln-Val-Gln-Val-Lys-Gln-His-Pro-Ile-Phe;

(7) P7: Tyr-Cys-Glu-Val-Pro-Ile-Asn-Phe-Ala-Met-Ala-Ala-Leu-Gly-Gly;

(8) P8: Pro-Ile-Asn-Phe-Ala-Met-Ala-Ala-Leu-Gly-Gly-Glu-Ile-Glu-Val;

(9) P9: Asn-Ser-Tyr-Tyr-Glu-Ile-Leu-Asp-Val-Pro-Arg-Ser-Ala-Ser-Ala;

(10) P10: Lys-Asp-Tyr-Tyr-Gln-Thr-Leu-Gly-Leu-Ala-Arg-Gly-Ala-Ser-Asp;

(11) P11: Thr-Thr-Tyr-Tyr-Asp-Val-Leu-Gly-Val-Lys-Pro-Asn-Ala-Thr-Gln;

(12) P12: Lys-Lys-Ala-Tyr-Arg-Arg-Lys-Ala-Leu-Gln-Trp-His-Pro-Asp-Lys;

(13) P13: Lys-Arg-Ala-Tyr-Arg-Arg-Gln-Ala-Leu-Arg-Tyr-His-Pro-Asp-Lys;

(14) P14: Lys-Lys-Ala-Tyr-Arg-Lys-Leu-Ala-Leu-Lys-Tyr-His-Pro-Asp-Lys;

(15) P15: Phe-Arg-Ser-Val-Ser-Thr-Ser-Thr-Thr-Phe-Val-Gln-Gly-Arg-Arg;

(16) P16: Pro-Gly-Met-Val-Gln-Gln-Ile-Gln-Ser-Val-Cys-Met-Glu-Cys-Gln;

(17) P17: Gly-Arg-Arg-Ile-Thr-Thr-Arg-Arg-Ile-Met-Glu-Asn-Gly-Gln-Glu;

(18) P18: Gln-Ala-Tyr-Glu-Val-Leu-Ser-Asp-Ala-Lys-Lys-Arg-Glu-Leu-Tyr-Asp;

(19) P19: Glu-Ala-Tyr-Glu-Val-Leu-Ser-Asp-Lys-His-Lys-Arg-Glu-

Ile-Tyr-Asp;
(20) P20: Ser-Gly-Pro-Phe-Phe-Thr-Phe-Ser-Ser-Ser-Phe-Pro-Gly-His-Ser;
(21) P21: Asp-Gly-Gln-Leu-Lys-Ser-Val-Thr-Ile-Asn-Gly-Val-Pro-Asp-Asp;
(22) P22: Asp-Leu-Gln-Leu-Ala-Met-Ala-Tyr-Ser-Leu-Ser-Glu-Met-Glu-Ala;
(23) P23: Glu-Asp-Leu-Phe-Met-Cys-Met-Asp-Ile-Gln-Leu-Val-Glu-Ala-Leu;
(24) P24: Leu-Cys-Gly-Phe-Gln-Lys-Pro-Ile-Ser-Thr-Leu-Asp-Asn-Arg-Thr;
(25) P25: Arg-Thr-Ile-Val-Ile-Thr-Ser-His-Pro-Gly-Gln-Ile-Val-Lys-His; and
(26) P26: Gly-Arg-Leu-Ile-Ile-Glu-Phe-Lys-Val-Asn-Phe-Pro-Glu-Asn-Gly.

INDEPENDENT CLAIMS are also included for the following:
(1) modulating an immune response in a subject by administering the immunogenic peptide portion of a dnaJ hsp to the subject;
(2) modulating immunoeffector cell responsiveness by contacting immunoeffector cells of a subject with the peptide portion of a dnaJ hsp cited above;
(3) a chimeric polypeptide comprising the peptide operatively linked to at least one heterologous polypeptide;
(4) a polynucleotide encoding the peptide;
(5) a recombinant nucleic acid molecule comprising the polynucleotide above operatively linked to at least one heterologous nucleotide sequence;
(6) a vector comprising the polynucleotide; and
(7) a cell containing the polynucleotide.

ACTIVITY - Immunomodulator; Cytostatic; Antiinflammatory; Antibacterial; Antiarthritic. No relevant biological data given.

MECHANISM OF ACTION - Interferon-Stimulator-Gamma; Tumor Necrosis Factor-Stimulator-Alpha; Interleukin-Stimulator-1; Interleukin-Stimulator-6; Interleukin-Stimulator-12; Interleukin-Stimulator-23; Interleukin-Inhibitor-4, Interleukin-Inhibitor-10, Transforming Growth Factor-Inhibitor-Beta; Interferon-Inhibitor-Gamma; Tumor Necrosis Factor- Inhibitor-Alpha; Interleukin- Inhibitor-1; Interleukin- Inhibitor-6; Interleukin-Inhibitor-12; Interleukin- Inhibitor-23; Interleukin- Stimulator-4, Interleukin- Stimulator-10, Transforming Growth Factor-Stimulator-Beta; Vaccine.

USE - The immunogenic peptide is useful for modulating (i.e. augmenting/inducing or reducing/inhibiting) an immune response in a subject having an immunological disorder (e.g. autoimmune disease), an infectious disease, an inflammatory bowel disease or cancer. The autoimmune disease is arthritis, specifically an articular juvenile idiopathic arthritis. The immunogenic peptide is also useful for modulating immunoeffector cell responsiveness in a subject (claimed). The immunogenic peptide is particularly useful for treating the above-mentioned diseases in mammals, e.g. cat, dog, horse, farm animal (e.g. ovine, bovine or porcine) or human. In general, the peptide is useful in methods involving mucosal tolerization, DNA vaccination, anergy induction or active immunization.

Dwg.0/26

L13 ANSWER 4 OF 34 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-163203 [21] WPIDS

CROSS REFERENCE: 1990-022380 [03]; 1995-036486 [05]; 2002-215020 [27]; 2003-298137 [29]
DOC. NO. CPI: C2002-050344
TITLE: Inducing or enhancing immune response in a patient by administering to the patient, a composition comprising an isolated fusion protein which comprises a stress protein or its part, fused to heterologous polypeptide.
DERWENT CLASS: B04 D16
INVENTOR(S): YOUNG, D; YOUNG, R A
PATENT ASSIGNEE(S): (WHED) WHITEHEAD INST BIOMEDICAL RES
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6335183	B1	20020101	(200221)*		29

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6335183	B1	CIP of	US 1988-207298	19880615
		Cont of	US 1989-366581	19890615
		CIP of	WO 1989-US2619	19890615
		CIP of	US 1991-804632	19911209
		CIP of	US 1993-73381	19930604
		CIP of	WO 1994-US6362	19940606
		Cont of	US 1994-336251	19941103
			US 1995-461722	19950605

PRIORITY APPLN. INFO: US 1994-336251 19941103; US 1988-207298 19880615; US 1989-366581 19890615; WO 1989-US2619 19890615; US 1991-804632 19911209; US 1993-73381 19930604; WO 1994-US6362 19940606; US 1995-461722 19950605

AN 2002-163203 [21] WPIDS
CR 1990-022380 [03]; 1995-036486 [05]; 2002-215020 [27]; 2003-298137 [29]
AB US 6335183 B UPAB: 20030505
NOVELTY - Inducing (M1) or enhancing immune response in a patient, comprising administering to the patient a pharmaceutical composition comprising an isolated fusion protein (I) having a stress protein or a portion of stress protein (Ia), fused to a heterologous protein or peptide (Ib), is new. (I) when administered to the patient, induces or enhances immune response against (Ib).

ACTIVITY - Virucide; Anti-HIV (human immunodeficiency virus); Antibacterial; Antiparasitic; Immunosuppressive; Antiarthritic; Antirheumatic.

MECHANISM OF ACTION - Immune response against heterologous enhancer or inducer (claimed).

The stress protein fusion vector pKS70 containing the T7 RNA polymerase promoter, a polylinker and the Mycobacterium tuberculosis heat shock protein (hsp)70 gene, was constructed. The human immunodeficiency virus (HIV) p24 gag gene was subcloned into pKS70 using the NdeI and BamHI sites and the resulting pKS72 vector was used to produce the p24-hsp70 fusion protein in **Escherichia**

coli. The fusion protein was purified as inclusion bodies and further purified using ATP-agarose chromatography and MonoQ ion exchange chromatography. The p24-hsp70 protein in phosphate buffered saline (PBS), in the absence of an adjuvant, was injected intraperitoneally into Balb/c mice. Three weeks later, the mice were boosted and finally, three weeks after the boost, the mice were bled. The anti-p24 antibody titer was then determined by enzyme linked immunosorbent assay (ELISA). Mice injected with 25 pmoles of p24-hsp70 had antibody levels 2.7 orders of magnitude higher than mice injected with p24 alone or hsp70 had antibody levels 2.7 orders of magnitude higher than mice injected with p24 alone or hsp70 alone. Results of the experiments in which mice were injected with p24 and the adjuvant, alum, also showed that there was an antibody response to p24. In addition, mice injected with the p24-hsp70 fusion protein and mice injected with p24 alone produced a demonstrable T cell response.

USE - For inducing or enhancing immune response in a patient against a heterologous protein or peptide which is administered as a part of the fusion protein which comprises a stress protein and the heterologous protein or peptide e.g. viral antigen such as an human immunodeficiency virus (HIV) protein or peptide e.g. gag or pol protein or peptide, preferably p24 protein or peptide, or a cancer antigen. (All claimed). (M1) is also useful for inducing or enhancing an individuals immune response to other pathogen such as bacteria, parasite, or other organism or agent such as toxins, toxoids. It is also useful for enhancing or inducing an upregulation of an individual's immune status (such as in an immune compromised individual or HIV-infected individual), and to decrease an individual's autoimmune response such as that which occurs in **rheumatoid arthritis**. The administration of the stress protein also provides protection against subsequent infection by a pathogen.

Dwg.0/7

L13 ANSWER 5 OF 34 SCISEARCH COPYRIGHT 2003 THOMSON ISI

ACCESSION NUMBER: 2002:776068 SCISEARCH

THE GENUINE ARTICLE: 592VU

TITLE: Major differences in antigen-processing correlate with a single Arg(71))-> Lys substitution in HLA-DR molecules predisposing to **rheumatoid arthritis** and with their selective interactions with 70-kDa heat shock protein chaperones

AUTHOR: Roth S; Willcox N; Rzepka R; Mayer M P; Melchers I (Reprint)

CORPORATE SOURCE: Univ Klinikum, Klin Forschergrp Rheumatol, Breisacher Str 64, D-79106 Freiburg, Germany (Reprint); Univ Freiburg, Clin Res Unit Rheumatol, Freiburg, Germany; Univ Freiburg, Inst Biochem & Mol Biol, Freiburg, Germany; Univ Oxford, John Radcliffe Hosp, Weatherall Inst Mol Med, Neurosci Grp, Oxford OX3 9DU, England

COUNTRY OF AUTHOR: Germany; England

SOURCE: JOURNAL OF IMMUNOLOGY, (15 SEP 2002) Vol. 169, No. 6, pp. 3015-3020.
Publisher: AMER ASSOC IMMUNOLOGISTS, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA.
ISSN: 0022-1767.

DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 38

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Several HLA-DR allelles are genetically associated with **rheumatoid arthritis**. DRB1*0401 predominates in Northern Europe and has a characteristic (70)QKRAA motif. This sequence contacts bound peptides and the TCR. Further interactions have been suggested with additional proteins during Ag loading. We explored the much stronger processing/presentation of full-length recombinant human acetylcholine receptor a subunit to a specific T cell clone by APC from DRB1*0401(+) than *0408(+) donors. Using DR*04 transfectants, we show that this difference results largely from the single Lys(71)<---->Arg interchange (0401<---->0408), which scarcely affects epitope binding, rather than from any other associated pollymorphism. Furthermore, we proved our recombinant polypeptides to contain the Eschetichia coli 70-kDa heat shock protein molecule Dnak and its requirement for efficient processing and presentation of the epitope by DRB1*0401(+) cells. According to a recent report, 70-kDa heat shock protein chaperones preferentially bind to the QKRAA, rather than the QRRAA, motif. Variations between the shared epitope motifs QKRAA and QRRAA are emphasized by underlining. We propose that such interactions enhance the intracellular epitope loading of *0401 molecules. They may thus broaden immune responses to pathogens and at least partially explain the distinct contributions of DRB1*0401 and other allelles to disease predisposition.

L13 ANSWER 6 OF 34 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2002216581 MEDLINE
DOCUMENT NUMBER: 21949629 PubMed ID: 11953969
TITLE: Interaction between heat-shock protein 73 and HLA-DRB1 alleles associated or not with **rheumatoid arthritis**.
AUTHOR: Auger Isabelle; Lepecuchel Lydia; Roudier Jean
CORPORATE SOURCE: INSERM EMI9940, Marseilles, France.
SOURCE: ARTHRITIS AND RHEUMATISM, (2002 Apr) 46 (4) 929-33. Journal code: 0370605. ISSN: 0004-3591.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020416
Last Updated on STN: 20020510
Entered Medline: 20020509

AB OBJECTIVE: HLA-DRB1 alleles whose third hypervariable region contains a QKRAA/QRRAA/RRRAA motif are associated with **rheumatoid arthritis** (**RA**) through unknown mechanisms. We previously demonstrated that the QKRAA motif was also expressed on the **Escherichia** coli 40-kd heat-shock protein (HSP) **DnaJ**. The QKRAA motif helps **DnaJ** bind its partner chaperone, the E coli 70-kd HSP DnaK. Furthermore, we observed that in lymphoblastoid cells, Hsp73, the constitutive 70-kd HSP, associates with HLA-DRB1*0401 (an allele with a QKRAA motif) and targets it to lysosomes. In this study, we sought to classify different HLA-DRB1 alleles according to their ability to bind Hsp73. METHODS: To evaluate how well different

HLA-DRB1 alleles could bind Hsp73, we developed a quantitative precipitation assay and a direct binding assay. RESULTS: Quantitative precipitation assay from total cellular proteins and from lysosomal extracts demonstrated that RA-associated HLA-DRB1 alleles bound Hsp73 better than did HLA-DRB1 alleles that were not associated with RA. HLA-DRB1*0401 was the best Hsp73 binder. These findings were confirmed by direct binding assay between purified proteins. CONCLUSION: HLA-DRB1*0401 was the best Hsp73 binder among the 8 different HLA-DRB1 alleles that were tested.

L13 ANSWER 7 OF 34 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2002271874 MEDLINE
DOCUMENT NUMBER: 22006984 PubMed ID: 12011974
TITLE: GIPC gene family (Review).
AUTHOR: Katoh Masaru
CORPORATE SOURCE: Genetics and Cell Biology Section, Genetics Division, National Cancer Center Research Institute, Tsukiji 5-chome, Chuo-ku, Tokyo 104-0045, Japan.. mkatoh@ncc.go.jp
SOURCE: INTERNATIONAL JOURNAL OF MOLECULAR MEDICINE, (2002 Jun) 9 (6) 585-9. Ref: 60
Journal code: 9810955. ISSN: 1107-3756.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020516
Last Updated on STN: 20020831
Entered Medline: 20020830

AB GIPC1/GIPC/RGS19IP1, GIPC2, and GIPC3 genes constitute the human GIPC gene family. GIPC1 and GIPC2 show 62.0% total-amino-acid identity. GIPC1 and GIPC3 show 59.9% total-amino-acid identity. GIPC2 and GIPC3 show 55.3% total-amino-acid identity. GIPCs are proteins with central PDZ domain and GIPC homology (GH1 and GH2) domains. PDZ, GH1, and GH2 domains are conserved among human GIPCs, Xenopus GIPC/Kermit, and Drosophila GIPC/ LP09416. Bioinformatics revealed that GIPC genes are linked to prostanoid receptor genes and **DNAJB** genes in the human genome as follows: GIPC1 gene is linked to prostaglandin E receptor 1 (PTGER1) gene and **DNAJB1** gene in human chromosome 19p13.2-p13.1 region; GIPC2 gene to prostaglandin F receptor (PTGFR) gene and **DNAJB4** gene in human chromosome 1p31.1-p22.3 region; GIPC3 gene to thromboxane A2 receptor (TBXA2R) gene in human chromosome 19p13.3 region. GIPC1 and GIPC2 mRNAs are expressed together in OKAJIMA, TMK1, MKN45 and KATO-III cells derived from diffuse-type of gastric cancer, and are up-regulated in several cases of primary gastric cancer. PDZ domain of GIPC family proteins interact with Frizzled-3 (FZD3) class of WNT receptor, insulin-like growth factor-I (IGF1) receptor, receptor tyrosine kinase TrkA, **TGF-beta** type III receptor (**TGF-beta** RIII), integrin alpha6A subunit, transmembrane glycoprotein 5T4, and RGS19/RGS-GAIP. Because RGS19 is a member of the RGS family that regulate heterotrimeric G-protein signaling, GIPCs might be scaffold proteins linking heterotrimeric G-proteins to seven-transmembrane-type WNT receptor or to receptor tyrosine kinases. Therefore, GIPC1, GIPC2

and GIPC3 might play key roles in carcinogenesis and embryogenesis through modulation of growth factor signaling and cell adhesion.

L13 ANSWER 8 OF 34 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2001-300515 [31] WPIDS
DOC. NO. CPI: C2001-092371
TITLE: Novel synthetic human target autoantigen gene useful for treating autoimmune diseases such as multiple sclerosis, insulin-dependent diabetes mellitus, **rheumatoid arthritis**, myasthenia gravis, and uveitis.
DERWENT CLASS: B04 D16
INVENTOR(S): BEN-NUN, A; KERLERO DE ROSBO, N; SAPPLER, G P
PATENT ASSIGNEE(S): (YEDA) YEDA RES & DEV CO LTD
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001031037	A2	20010503	(200131)*	EN	182

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001010510 A 20010508 (200149)
EP 1238089 A2 20020911 (200267) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001031037	A2	WO 2000-IL688	20001026
AU 2001010510	A	AU 2001-10510	20001026
EP 1238089	A2	EP 2000-971684	20001026
		WO 2000-IL688	20001026

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001010510	A	Based on	WO 200131037
EP 1238089	A2	Based on	WO 200131037

PRIORITY APPLN. INFO: IL 1999-132611 19991027
AN 2001-300515 [31] WPIDS
AB WO 200131037 A UPAB: 20010607
NOVELTY - A synthetic human target autoantigen gene (I) that comprises sequences coding for at least two immunogenic epitopic clusters (IEC) of autoantigen(s) related to a specific autoimmune disease, is new.
DETAILED DESCRIPTION - (I) is selected from:
(a) a synthetic human target autoantigen gene (shTAG) comprising nucleotide sequences coding for at least two IECs of a

sole autoantigen related to the autoimmune disease;

(b) a synthetic human multitarget autoantigen gene (shMultiTAG) comprising nucleotide sequences coding for at least one IEC of at least two different autoantigens related to the autoimmune disease; and

(c) a nucleotide sequences homologous, complementary or hybridizable to shTAG or shMultiTAG, provided that the expressed polypeptide retains its immunogenic, and more preferably, its **immunomodulatory** activity.

INDEPENDENT CLAIMS are also included for the following:

(1) a synthetic polypeptide (II) that comprises amino acid sequences of at least two IEC of autoantigens related to a specific autoimmune disease, where (II) is selected from:

(a) a synthetic human polypeptide (shPEP) comprising amino acid sequences of at least two IECs of a sole autoantigen related to the autoimmune disease;

(b) a synthetic human multitarget polypeptide (shMultiPEP) comprising amino acid sequences of at least one IEC of at least two different autoantigens related to the autoimmune disease; and

(c) an analog of shPEP or shMultiPEP obtained by substitution, variation, modification, replacement, deletion, or addition of one (or more) amino acid residues from or to the sequences of the polypeptide, provided that immunogenicity or more preferably, the **immunomodulatory** activity of the IEC is retained;

(2) a pharmaceutical composition (III) comprising (II), or (I) and a suitable gene delivery vehicle for delivery of (I) to a target cell population ex vivo or in vivo; and

(3) a diagnostic composition (IV) comprising (I) or (II), for diagnosis and/or monitoring the progression of an autoimmune disease.

ACTIVITY - Antidiabetic; antirheumatic; antiarthritic; neuroprotective; ophthalmological; antiinflammatory; hepatotropic; antithyroid; hemostatic; antiulcer.

MECHANISM OF ACTION - **Immunomodulator**. Injections of Y-MSPa protected SJL/J mice against EAE induced with PLP139-151. SJL/J mice were injected with 200 micro l of emulsion containing 150 micro g PLP139-151 in CFA supplemented with 200 micro g Mycobacterium tuberculosis. On days 5, 7, 9 and 11 after the encephalitogenic challenged, mice received injections of 500 micro l phosphate buffered saline (PBS) alone or PBS containing 200 micro g PLP139-151, 200 micro g Y-MSPa, or 200 micro g shMOG/E. Mice were scored daily for clinical signs. Administration of a soluble aqueous form of Y-MSPa after induction of EAE with PLP139-151 abrogated disease development in SJL/J mice. The data indicated that administration of Y-MSP in a soluble form **immunomodulates** potentially pathogenic autoreactive T-cells.

USE - (I), (II) or (III) is useful for treating autoimmune diseases such as multiple sclerosis, insulin-dependent diabetes mellitus, **rheumatoid arthritis**, myasthenia gravis, uveitis (claimed), autoimmune hepatitis, thyroiditis, insulitis, orchitis, idiopathic thrombocytopenic purpura, and inflammatory diseases (Crohn's disease, ulcerative colitis). (I) and (II) are also useful for diagnosis and/or monitoring the progression of the autoimmune disease.

Dwg.0/61

L13 ANSWER 9 OF 34 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2001168525 MEDLINE

DOCUMENT NUMBER: 21166269 PubMed ID: 11269727
TITLE: Immunodominant region of Actinobacillus actinomycetemcomitans 40-kilodalton heat shock protein in patients with **rheumatoid arthritis**.
AUTHOR: Yoshida A; Nakano Y; Yamashita Y; Oho T; Ito H; Kondo M; Ohishi M; Koga T
CORPORATE SOURCE: Department of Oral and Maxillofacial Oncology, Kyushu University, Faculty of Dental Science, Fukuoka, Japan.. aki@dent.kyushu-u.ac.jp
SOURCE: JOURNAL OF DENTAL RESEARCH, (2001 Jan) 80 (1) 346-50. Journal code: 0354343. ISSN: 0022-0345.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Dental Journals; Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010410
Last Updated on STN: 20010410
Entered Medline: 20010405

AB Bacterial heat shock proteins have been implicated in the pathogenesis of several diseases, and the immunological relationship between **rheumatoid arthritis** (**RA**) and **Escherichia** coli **DnaJ** has been reported. Since there are similarities in the tissue destruction process of RA and periodontitis, we examined the reactivities of antibodies in sera from RA patients to the **DnaJ** protein from Actinobacillus actinomycetemcomitans. An enzyme-linked immunosorbent assay showed that IgG titers to the N-terminal conservative region of the **DnaJ** are significantly higher in RA patients compared with the healthy controls ($p < 0.05$). Furthermore, we examined IgG titers of disease controls to determine the specificity of the immune responses to this region in RA patients. The difference between RA and infectious disease patients was also significant ($p < 0.05$). These results suggest that the N-terminal region of **DnaJ** from A. actinomycetemcomitans may contribute to the etiologic analysis of RA.

L13 ANSWER 10 OF 34 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:231031 BIOSIS
DOCUMENT NUMBER: PREV200100231031
TITLE: The exchange of one single amino acid at position 71 of the DR4 beta-chain leads to significant differences in antigen processing and presentation of a human autoantigen chaperoned by a member of the HSP70 family.
AUTHOR(S): Roth, Sabine (1); Willcox, Nicholas; Mayer, Matthias P.; Melchers, Inga (1)
CORPORATE SOURCE: (1) Clinical Research Unit for Rheumatology, University Medical Center, Freiburg Germany
SOURCE: European Journal of Immunogenetics, (April, 2001) Vol. 28, No. 2, pp. 220. print.
Meeting Info.: 15th European Histocompatibility Conference Granada, Spain March 27-30, 2001
ISSN: 0960-7420.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L13 ANSWER 11 OF 34 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:83091 BIOSIS
DOCUMENT NUMBER: PREV200100083091
TITLE: HSP40 and chronic autoimmune disease.
AUTHOR(S): Thompkins, P. B. (1); Krzewski, K.; Griffiths, B.; Emery, P.; Lipinska, B.; Lindsey, N. J. (1); Ashraf, W. (1)
CORPORATE SOURCE: (1) Department of Biomedical Sciences, University of Bradford, Bradford, BD7 1DP UK
SOURCE: Immunology, (December, 2000) Vol. 101, No. Supplement 1, pp. 105. print.
Meeting Info.: Annual Congress of the British Society for Immunology Harrogate, UK December 05-08, 2000 British Society for Immunology
. ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L13 ANSWER 12 OF 34 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1999334399 MEDLINE
DOCUMENT NUMBER: 99334399 PubMed ID: 10405927
TITLE: Isolation of an IgG monoclonal anti-**dnaJ** antibody from an immunoglobulin combinatorial library from a patient with **rheumatoid arthritis**.
AUTHOR: Chukwuocha R U; Zhang B; Lai C J; Scavulli J F; Albani S; Carson D A; Chen P P
CORPORATE SOURCE: Department of Medicine, University of California, Los Angeles 90095-1670, USA.. rchukwu@ucla.edu
CONTRACT NUMBER: AR41897 (NIAMS)
HL03523 (NHLBI)
SOURCE: JOURNAL OF RHEUMATOLOGY, (1999 Jul) 26 (7) 1439-45.
Journal code: 7501984. ISSN: 0315-162X.
PUB. COUNTRY: Canada
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991221

AB OBJECTIVE: Previously, we showed that **rheumatoid arthritis** (**RA**) had both antibodies and T cells specific for the QKRAA-encompassing **Escherichia** coli **dnaJ** protein. These findings suggest that the bacteria induced anti-**dnaJ** responses may cross react with the human homolog of bacterial **dnaJ** in the joint, resulting in tissue damage. METHODS: We used the combinatorial library technique to isolate and characterize an IgG monoclonal anti-**dnaJ** antibody (designated CG1) from the blood of a patient with RA. RESULTS: Sequence analysis of CG1 revealed that its heavy and light chain V regions were respectively most homologous to the 3d279d VH4 and the O18 Vk1 genes. Interestingly, 3d279d is frequently expressed by B cells stimulated with staphylococcal enterotoxin; and O18 is the main gene employed by the Vk1 IgG antibodies against Haemophilus influenzae. CONCLUSION: The combinatorial

immunoglobulin library method represents an interesting model of how to approach the isolation and characterization of antibody-like reagents in the elucidation of autoantigens in RA.

L13 ANSWER 13 OF 34 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 1999:360361 SCISEARCH
THE GENUINE ARTICLE: 192QM
TITLE: Evidence that patients with **rheumatoid arthritis** have asymptomatic 'non-significant' **Proteus** mirabilis bacteriuria more frequently than healthy controls
AUTHOR: Senior B W (Reprint); Anderson G A; Morley K D; Kerr M A
CORPORATE SOURCE: UNIV DUNDEE, NINEWELLS HOSP & MED SCH, DEPT MED MICROBIOL, DUNDEE DD1 9SY, SCOTLAND (Reprint); UNIV DUNDEE, NINEWELLS HOSP & MED SCH, DEPT MED, DUNDEE DD1 9SY, SCOTLAND
COUNTRY OF AUTHOR: SCOTLAND
SOURCE: JOURNAL OF INFECTION, (MAR 1999) Vol. 38, No. 2, pp. 99-106.
Publisher: W B SAUNDERS CO LTD, 24-28 OVAL RD, LONDON NW1 7DX, ENGLAND.
ISSN: 0163-4453.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 28

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Objectives: patients with **rheumatoid arthritis** (**RA**) are reported to have in their sera raised levels of antibody specific to **Proteus** mirabilis. The aim of the study was to verify this and to determine an explanation for it by investigating the frequency of P. mirabilis urinary tract infection in **RA** patients and matched controls.

Methods: freshly voided urine was examined for the presence, number and identity of infecting bacteria. The levels of antibody in blood and in urine of the IgM, IgA and IgG classes to the common O serotypes of P. mirabilis and the antigens to which they reacted were determined by enzyme-linked immunosorbent assay (ELISA) and immunoblotting.

Results: analysis of urine from 76 patients with RA and 48 age- and gender-matched healthy controls showed that only two (4%) of the control urines but 25 (33%) of those fi om the RA patients were infected. The commonest infecting organism in the RA patients' urine was **Proteus** mirabilis which occurred twice as frequently as **Escherichia** coli. **Proteus** mirabilis was found in 52% of the infected urines of the RA patients and was always detected as a pure growth and usually in insignificant (< 10(4)/ml) numbers. It is highly improbable that this finding was the outcome of differences in age, physical ability or medication between the RA and control patient groups. Comparison of antibody levels to P. mirabilis by ELISA showed RA patients had raised ($P < 0.0001$, $P = 0.001$, $P = 0.0063$) levels of IgA, IgG and IgM respectively in their sera and raised ($P < 0.0001$, $P < 0.0001$, $P = 0.0001$) levels of IgG, IgM and IgA respectively in their urine compared with the control group. It was not possible to detect an antibody reacting to a P. mirabilis antigen that was specific to the RA patients.

Conclusion: the results confirm that RA patients have raised

levels of antibody to P. mirabilis not only in blood but also in urine and suggest that this arises because RA patients have an asymptomatic, non-significant P. mirabilis bacteriuria more frequently or more prolonged than control patients. This may be the trigger for their RA condition.

L13 ANSWER 14 OF 34 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 1998:268474 SCISEARCH
THE GENUINE ARTICLE: ZE588
TITLE: Mucosal modulation of immune responses to heat shock proteins in autoimmune arthritis
AUTHOR: Bonnin D (Reprint); Albani S
CORPORATE SOURCE: UNIV CALIF SAN DIEGO, DEPT PEDIAT, 9500 GILMAN DR, LA JOLLA, CA 92093 (Reprint); UNIV CALIF SAN DIEGO, DEPT MED, LA JOLLA, CA 92093
COUNTRY OF AUTHOR: USA
SOURCE: BIOTHERAPY, (MAR 1998) Vol. 10, No. 3, pp. 213-221. Publisher: KLUWER ACADEMIC PUBL, SPUIBOULEVARD 50, PO BOX 17, 3300 AA DORDRECHT, NETHERLANDS. ISSN: 0921-299X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 39

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Induction of oral tolerance to antigens that are targets of self-reactive immune responses is an attractive approach to antigen-specific immune therapy of autoimmune diseases. Oral tolerization has indeed proven to be safe and effective in amelioration of autoimmune diseases in animal models, In humans, results have been somewhat controversial. The emphasis given to clinical outcome rather than to **immunomodulation**, and the difficulty in identifying appropriate candidate antigens contribute to the controversy. Heat shock proteins are promising targets for immune intervention. Immune reactivity to heat shock proteins has indeed been correlated with autoimmune arthritis in animal models, and abnormal immune responses to heat shock proteins have been described in human arthritis as well. Despite significant recent progress, little is known at a molecular level regarding the mechanisms which are responsible for a switch from autoimmunity to tolerance in humans. This is particularly true with respect to sequential analysis of several molecular and immunologic markers during both the course and treatment of disease. Novel approaches are currently under way to fill the gaps. We will briefly detail here the experience gained to date, and identify some of the avenues which future research will explore.

L13 ANSWER 15 OF 34 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 97263510 MEDLINE
DOCUMENT NUMBER: 97263510 PubMed ID: 9109425
TITLE: A function for the QKRAA amino acid motif: mediating binding of **DnaJ** to DnaK. Implications for the association of **rheumatoid arthritis** with HLA-DR4.
AUTHOR: Auger I; Roudier J
CORPORATE SOURCE: Laboratoire d'Immuno Rhumatologie, Faculte de Medecine de Marseille, France.
SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (1997 Apr 15) 99